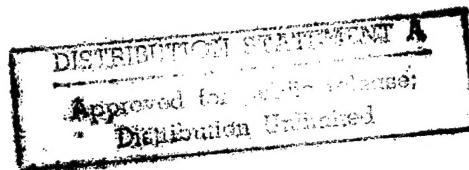


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Vol 19, No 3, May-June 1985

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14 August 1985

# USSR REPORT

## SPACE BIOLOGY AND AEROSPACE MEDICINE

Vol. 19, No 3, May-June 1985

Translation of the Russian-language bimonthly journal  
KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA  
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## EDITORIAL

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FORTIETH ANNIVERSARY OF THE SOVIET PEOPLE'S VICTORY IN THE GREAT PATRIOTIC WAR, AND AVIATION MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 8 Jan 85) pp 4-7

[Article by N. M. Rudnyy]

[Text] The Soviet people and all of progressive mankind are celebrating this year the 40th anniversary of the victory in the Great Patriotic War of 1941-1945.

It would be impossible to exaggerate the worldwide historical significance of this victory. The most reactionary and aggressive forces of worldwide imperialism--fascist Germany and then militaristic Japan, which set as their goal to erase the world's first socialist state from the face of the earth--were defeated. Thus, mankind was rid of fascist slavery. The Soviet people were able to restore the devastated national economy and undertake the building of developed socialism. Many of the peoples liberated from the fascist yoke selected the socialist route of development. There was an enormous swing all over the world toward the national liberation and workers' movement, struggle for genuine democracy, peace and socialism. The balance between capitalism and socialism on our planet has changed radically in favor of socialism.

The farther back in history that years recede, the more vividly we view the great feat of the Soviet people and their Armed Forces which, under the leadership of the Communist Party of the Soviet Union, defended freedom, honor and independence of their homeland, displayed heroism on a mass scale, inexhaustible will to win, persistence and infinite courage in the rigorous trials and fatal battles against brutal fascism in the most bitter and bloody war in the history of mankind.

Our Air Force has also written many glorious pages in the history of the Great Patriotic War. Soviet eagles, the courageous sons of their homeland, defeated the enemy in air combat, assaulted materiel and fascist troops, won supremacy in the air, protecting and supporting ground troops in their victorious advance.

The foundation and conditions for scientific and technological progress and the combat skill of our aviation were laid long before the war. The Communist Party and Soviet government constantly devoted much attention to aviation, which

always held on the leading places in the world. The conquest of high altitudes and flying speed, long-distance flights in Europe and Asia, the rescue of participants in the Chelyuskin expedition and flights over the North Pole to America--all these heroic deeds of the prewar years were landmarks in the progress of our aviation that determined its technical and combat assistance during the Great Patriotic War.

Soviet aviation medicine developed together with Soviet aviation. At the personal instructions of V. I. Lenin, the first aviation detachment was formed in 1917 and in 1920, the regular post of aviation physician was introduced. In subsequent years, aviation medicine developed at an accelerating pace: scientific research and scientific-clinical institutions were founded, combined and individual aviation medicine problems of importance to aviation were solved.

In the second half of the 1930's, the Institute of Aviation Medicine of the Workers' and Peasants' Red Army imeni I. P. Pavlov, Military Medical Academy imeni S. M. Kirov and Central Psychophysiological Laboratory of the USSR Civil Air Fleet became the main scientific centers in the USSR that dealt with aviation medicine. The work of these institutions covered the entire range of problems of aviation medicine.

At its inception, Soviet aviation medicine made extensive use of the achievements of Soviet physiology, hygiene and the entire set of clinical disciplines in the area of both theory and methodological investigative procedures. The greatest Soviet medical scientists offered much help to the pioneers in Soviet aviation medicine in its formation.

Thus, the formation and development of aviation medicine in the USSR is inseparably linked with the victory of the Great October Socialist Revolution, establishment of the Air Force of our homeland, progress in Soviet aviation, achievements of Soviet theoretical and clinical medicine.

The rapid development of aviation equipment in the prewar period advanced to the fore such prominent problems as altitude and speed. The problem of altitude, i.e., medical support of safe flights at high (up to 12,000 m) altitudes involved work in the following directions: investigation of the effects of different degrees of hypoxic hypoxia on vital functions and analyzer systems of the body; investigation of mechanisms of regulation and adaptation to this factor; search for means of enhancing tolerance to hypoxia and its prevention. Investigations in this direction were pursued mainly at the Institute of Aviation medicine, in departments of the Military Medical Academy imeni S. M. Kirov and the Central Psychophysiological Laboratory of the Civil Air Fleet. As a result of these investigations, some fundamental data were obtained on etiopathogenesis of hypoxic states among flight personnel during flights, which made it possible to develop a number of effective means of protection against hypoxia. Thus, determination was made of the main physiological and hygienic specifications for oxygen instruments and pressurized cabins of a small size for different types of aircraft of that time, and this was the basis for all subsequent developments in this direction.

Before the war, investigation of the effects of accelerations on man was a rather important problem of aviation medicine. By that time, high-speed and highly maneuverable aircraft had appeared in the Air Force, in which the performance of intricate aerobatics generated high accelerations. In spite of the limited technical capabilities of investigation, the first and rather important data, from the practical point of view, were obtained concerning tolerance to accelerations as related to their direction. The results of these studies demonstrated the desirability of special conditioning of flight personnel to enhance their resistance to accelerations. The recommendations elaborated on this score made it possible to develop a set of measures, which found wide use in Air Force units [chasti].

Concurrently, there were clinicophysiological studies of the problem of flight work, its effect on the health of flight personnel, determination of occupational hazards and setting standards. They served as the basis for regulating the flight load and developing the basic theses of medical flight expertise. Scientific research institutions of Soviet aviation medicine worked in constant contact with the aktiv of army aviation physicians, making use of their rich practical experience.

In assessing the prewar period of Soviet aviation medicine, it can be concluded that it was rather well-prepared for medical support of combat operations of the Air Force to defend our homeland against fascist aggression.

The achievements made in the area of scientific research and accumulated experience in medical support of flights laid a solid theoretical foundation for organization of medical support of combat operations of aviation during the Great Patriotic War.

The onset of the Great Patriotic War altered the direction of work and organizational forms of aviation medicine. Two basic tasks for Soviet aviation medicine emerged distinctly: to assure high efficiency of flight personnel during tense combat operations; strive for fullest and speediest return to the ranks of temporarily disabled Air Force personnel.

The Central Aviation Hospital, which was governed in its work by army aviation hospitals, became the center for all therapeutic and expert medical work. New criteria and methods were developed for medical flight expertise, methods were sought to eliminate and prevent fatigue of flight personnel; the modes of using oxygen during long-term night flights were defined; practical training was offered for high-altitude flights for flight crews that were protecting the capital of our homeland against the fascist vultures.

Effective organizational guidelines for building the medical service of the Air Force, distribution of its personnel and resources, and the adopted system of medical evacuation in stages assured the preservation of qualified flight cadres and their speedy return to active duty (at the start of the war, special departments were opened for treatment of flight personnel at evacuation hospitals, then army aviation hospitals, and in 1942 the Central Aviation Hospital was founded). In the entire period of the Great Patriotic War, the largest volume of medical care and treatment of flight and technical

personnel was rendered in troop infirmaries of aviation ground service units (80-85% of all the wounded and sick). In 1943-1945, up to 75% of the flight personnel and 80.2% of the technical personnel were returned to active duty from such infirmaries of some troop formations [ob'yedineniye].

Replacements in the ranks of the active army were made to a significant extent by returning to duty those who were temporarily removed due to injury or illness. Expressly this task was apparently the most important one for the Air Force, if we consider the specifics of the flying profession. The extensively used system of evacuating casualties by air was instrumental in its successful solution.

By the start of the war, we already had considerable experience in using both ambulance aircraft and military aircraft that had been specially equipped and adapted. Thus, evacuation of casualties by air transport proceeded successfully during the military events on Lake Khasan and during the war in Spain. The experience in transporting wounded pilots from Spain over long distances (2000-2200 km) and at altitudes of up to 5000 m is very interesting.

Prewar experience in using ambulance aircraft made it possible to test in practice the validity of previously elaborated indications and contraindications for transporting casualties via aircraft. All this knowhow turned out to be quite useful in organizing the work of the medical aviation during the Great Patriotic War.

Analysis of the performance of the medical service of the Air Force--all of its elements, including scientific research institutions--during the 1941-1945 period of the Great Patriotic War revealed that Soviet aviation medicine coped well with the tasks put to it and, consequently, had performed its duty to its homeland.

The postwar period was characterized by rapid development of aircraft. Jet engines came to replace piston engines in aircraft building. There was drastic increase in speed and altitude of flights. New types of flying machines appeared. Development of aviation equipment was associated with constant increase in influence of flight factors and in demands made upon pilots.

Aviation medicine was faced with a number of new problems, while the solution of former ones required a deeper approach and consideration of new aspects.

In view of the increasing speed and altitude of flights, the problem of their safety became considerably more complex. It was necessary to develop new methods and principles of rescuing flight crews in the event of emergency situations. As a result of comprehensive research and investigations on the effects on man of long-term and impact accelerations, a method was developed of forced abandonment of aircraft over the entire range of flying speeds. However, this method (ejection) did not assure complete safety at high altitudes, since it did not preclude onset of acute hypoxic hypoxia and decompression disorders. In order to eliminate such a danger, new methods were developed to supply oxygen (breathing under positive pressure) and special high-altitude gear (cockpit oxygen equipment and space suits).

We should mention noise trauma and vibration among the other problems that were worked on with success in the postwar period. The results of investigations conducted in this direction made it possible to validate standards and develop personal and group protection measures against deleterious factors.

All of the scientific research pursued by aviation medicine was ultimately directed toward finding the means of protecting crews against diverse adverse flight factors (hypoxia, changes in barometric pressure, accelerations, noise, vibration, etc.), assuring high efficiency of flight personnel and safety of flights in new aviation equipment.

The rising development of aviation equipment, expansion of problems being solved by aviation, performance of flights at any time of day and in any weather increased significantly the requirements as to a pilot's health status and psychophysiological qualities.

A more refined system of constant medical monitoring of flight personnel became necessary. Monitoring of flight personnel during flights acquired much importance.

Medical and psychological screening of cadets for flight training, validation of requirements of medical flight expertise on subjects allowed to do flight work have considerable significance in the overall system of medical support of flights. Medical tactics are constantly being upgraded in the light of the latest advances of medicine. Much attention is devoted to medical rehabilitation, retaining flight personnel on the job and returning those who have had different diseases to their flight jobs.

Flight practice also required a revision of the entire set of preventive measures, search for additional ways and methods of conditioning the body that are aimed at increasing endurance and efficiency of pilots in flight, and formation in them of professional qualities. The question was raised of offering special psychophysiological training to flight personnel.

The increasing complexity of aviation equipment and radical increase in its tactical flying features made it necessary for aviation medicine to concentrate on the study of psychophysiological performance of crews and functional capacities of man. Aviation physicians, together with specialists in engineering psychology, are pursuing much research for scientific validation of specifications for flight vehicles, their systems and complexes, on the basis of man's psychophysiological capabilities and distinctions of his work. Investigations in this direction help optimize and increase the reliability of the human element in the pilot-aircraft system.

Investigation of working conditions of engineering, technical and other personnel who implement flights and development of recommendations to safeguard their health occupy a significant place in modern aviation medicine. In particular, much attention is devoted to the study of psychophysiological performance and medical support of personnel who control air traffic.

In the 40 years that have elapsed since the heroic days of the Great Patriotic War, our country under the guidance of Lenin's Communist Party has healed its wounds and restored the devastation inflicted by the war, it has made remarkable advances in the economic, sociopolitical and spiritual development of society, as well as in strengthening the power of the socialist state. Soviet people are consistently and systematically implementing the program for peace and creativity elaborated by the 26th Party Congress.

Scientific and technological achievements are being introduced to the practice of modern aviation with increasing breadth and depth. The power of military materiel has grown immeasurably. The once menacing Yaks, Migs, IIs and other combat machines of the Great Patriotic War have been replaced with new generations of aircraft.

Aviation medicine is conducting its investigations on a high modern level, making the needed contribution to development of aviation, support of complicated flights, crew training, development of the scientific conditions for fruitful and creative performance by a new generation of pilots, to assure their good health and professional longevity.

## SURVEY

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629.78:612.014.426.014.49

### ELECTROMAGNETIC RADIOFREQUENCY (MICROWAVE) RADIATION: GUIDELINES, CRITERIA FOR SETTING STANDARDS AND 'THRESHOLD' DOSE LEVELS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 2 Nov 83) pp 8-21

[Article by B. I. Davydov]

[English abstract from source] This paper discusses the principles and criteria of standardization of electromagnetic radiation in the radiofrequency range. The concept of risk as a standardization criterion normally used in the radiobiology of ionizing radiation can also be employed in the standardization of electromagnetic radiation. It is recommended to use as major parameters of "harmfulness" longevity, cataract formation and genetic effects in vivo as well as mortality rate in the laboratory experiment. The value of 0.1% is taken for the primary risk level. The paper describes approaches to the extrapolation of experimental data concerning threshold effects. As follows from pertinent calculations, the specific absorption of the electromagnetic dose rate for the personnel is 0.4 W/kg during one hour exposure.

[Text] The relationship between equipment and man's environment indicates that they cease to develop as separate systems, evolving into a single industry-environment system [15]. Aviation and cosmonautics emerge as part of this metasystem.

Modern aviation and space equipment cannot manage without sources of electromagnetic radiation (EMR) in radiofrequency and microwave range,\* which is very wide, from critically low (ultra long-range) to critically high frequencies (RLS [radar stations] with high resolution).

Guidelines: G. I. Sidorenko and M. A. Pinigin [18] refer the following to the basic principles for setting standards: complex, combined effect of physical and chemical factors of technogenic and natural origin, probabilistic approach to evaluation of levels of effect, consideration of adaptability of the body, evaluation of actual and maximum allowable burden (MAB),

\*Referred to hereafter as only EMR.

The biomedical aspects imply evaluation of significant biological effects and determination of correlation between EMR level and effect. Determination is made of levels or values of EMR that are "harmless" or acceptable for different categories of people who are in contact with this factor on the basis of medical and social considerations. In the case of technogenic standardization, the "deleteriousness" of this factor sometimes recedes to the background, since one has to make a choice between the probability of harming an individual and the economic advantage promised by acceptance of less stringent standards.

Optimization and ergonomics of standard-setting require their own methodology. There is the special question of criteria and risk levels of proposed standards or assessment of risk in the case of accidental overexposure. Participation of not only medical specialists and biologists, but also sociologists and philosophers is required to settle the question of harm (harmlessness)--benefit (gain). This is a difficult deontological problem [19]. At the present time, the harm-benefit formula is examined through the conception of risk. It obtained the most development in radiobiology of ionizing radiation [4, 12, 14, 28, 34]. These ideas are quite acceptable for setting EMR standards as related to occupational activities. However, one encounters major problems of a moral and ethical nature in setting them for the population. In the opinion of the leading hygienists in our country, the conception of "acceptable" risk is generally unacceptable in this case [19].

Setting standards is a largely social process. For this reason, one has to revise adopted standards in most cases. Of course, along with the question of validity of new proposals, one should also consider the counterquestion valid: Was the old approach sufficiently validated?

When setting standards for EMR in the case of occupational activity, one can take three criteria: operator's efficiency or labor productivity, somatic health status and genetic sequelae. The latter is particularly important to consider when setting standards for the public in the area of action of electromagnetic sources (RLS, tropospheric communication, television, radio, etc.).

Social factors, as well as moral and ethical principles, to which adhere specific individuals holding key positions in this area, also have a rather appreciable effect on the choice of a criterion and, consequently, biological equivalent.

Not all specialists are equally knowledgeable about the problem of setting a standard for this factor, its social and economic importance. However, they all believe that the existing approaches to standardization require thorough analysis and economically (socially) justified EMR standards. It is particularly important to take this into consideration when solving technical problems related to aviation and space equipment.

Thus, there are major difficulties in the problem of standardization. The specialists working in this field encounter biomedical, technical, economic and sociopsychological problems. The latter are particularly difficult,

since they must be based on modern interpretations of such concepts and categories as health and disease, normal and pathology, population and individual [15].

**Criteria. Dose levels:** One can single out at least four dose levels and, accordingly, four concepts: dose limit, tolerated or maximum allowable dose, warranted risk dose and critical dose. When considering the effect of ionizing radiation on the public, one uses the concept of "dose limit." The concept of "maximum allowable dose" is limited to occupational exposure according to current international and national recommendations and ionizing radiation safety.

The last two dose categories can apply only to occupational exposure. The basic ideas and approaches to standardizing EMR could, with minor allowances, be taken from radiobiology of ionizing radiation. These two types of radiation have many features in common with regard to phenomenology of phenomena (biological effects) [8]. Moreover, the very approach to quantitative evaluation using a criterion such as mortality is also taken from radiobiology of ionizing radiation. The theses cited below on setting standards for EMR are similar in many respects with views in the works of Ye. I. Vorob'yev, Yu. G. Grigor'yev, Ye. Ye. Kovalev, Yu. I. Moskalev and others [4, 7, 12, 14], as well as the recommendations of ICRP [International Commission on Radiological Protection] pertaining to ionizing radiation. Whatever we call some dose level (dose limit, maximum allowable burden, tolerated dose, dose of justified risk, critical dose), the question is not about terminology. It is important to establish the purpose and conditions under which specific doses will occur and how many people are exposed to radiation.

A gradation of dose levels can be determined for the following categories of people: the entire population unrelated to EMR by occupation (dose limit); individuals whose occupation involves EMR--ordinary working conditions (tolerated or maximum allowable dose); individuals whose occupation is related to EMR--extreme conditions, repair work in accident situations (justified risk dose). Of course, pilots and cosmonauts must be classified in the last two categories.

One can consider dose gradations in an alternative aspect: the more important the work being done, functional duties or operator's task, the lower the dose level must be.

At the present time, the maximum allowable dose for man is considered to be one that, in the light of current knowledge, "involves a rather insignificant possibility of serious somatic and genetic sequelae" [7]. Of the somatic consequences, primarily reduction of life span, leukemia and other malignant neoplasms, cataract are particularly significant for large population groups. These effects can be detected only by means of statistical methods of analysis.

Standards of radiation safety for ionizing radiation were developed using basically the same approaches, and they did not differ appreciably in different countries. On the basis of recommendations of international committees and organizations (ICRP, WHO, IAEA [International Atomic Energy Agency]), national

organizations developed standards for their countries which, unfortunately, was not the case until recently [31] for standardization of EMR.

In order to estimate the "threshold" dose levels of EMR for professionals and the public, it is necessary, first of all, to have good information about the biological effect as a quantitative function of radiation dose. It is important to select appropriate criteria and risk levels. For EMR, one can take the following criteria: cataractogenic effect, reduction of life span, impairment of heat balance and lethal effects (applicable in animal experiments). Most of these criteria are based on experimental data.

If we assume that the cataractogenic effect of EMR can indeed be demonstrated in man, one could take as the risk level double the incidence of spontaneous cataract in the population or the cataractogenic effect of ionizing radiation in permissible doses for professionals. Reduction of life span, leukemia, cancer and genetic effects on man are standardization criteria that are difficult to assess. One could use the level of overheating that does not elicit appreciable changes in the cardiovascular and respiratory systems as the tolerated level of impairment of thermal balance with EMR. The last criterion, however, mortality rate, requires other approaches that are based on the conception of acceptable risk that is used in radiobiology of ionizing radiation [4, 7, 12, 14, 28, 34].

One can try to find the methodology for determining the relevant dose levels according to different criteria of risk. The dose of justified risk is any dose of radiation that becomes active in extreme, accident situations and is comparable to an existing risk [8]. In the opinion of ICRP, it would be unrealistic to recommend any dose limits in extreme situations. This is justified by the task of saving the lives of the rest of the people.

Risk as a stochastic standardization criterion: At the present time, much attention is devoted to validation of dose standards by means of thorough analysis of information about risk in different areas of human endeavor. Risk is assessed in general biological, medical, economic and social aspects [4, 12, 14, 28, 34].

When discussing use of the conception of risk, one should give special attention to quantitative relations between risk of different manifestations of exposure to EMR and exposure dose.

Ideally, the level of acceptability of risk for professionals should conform to equilibrium between health, risk and benefit. Risk as applied to an individual always seems higher than if the same risk is considered somewhat objectively and in estimating the risk for large groups of people or a country's population as a whole. The conception of risk can be socially

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\*Not only biomedical, but social meaning is placed in the concept of "threshold" dose levels. For this reason, use of "threshold" in the medical sense is rather arbitrary.

acceptable only if all the "pros" and "cons" are taken into consideration, if this conception is not in contradiction to the basic social and moral-ethical sets of society.

Mortality rate as the highest risk category: Risk is an inseparable element of a man's existence. It is determined by evolution and ensues from the basic laws of everything living--birth and death as the highest category of risk. Risk is a probabilistic concept. According to the WHO definition listed in its by-laws, health is a state of complete physical, mental and social wellbeing, rather than merely the absence of disease, trauma or physical defects. In terms of risk, one can refer to an acceptable level of wellbeing.

Table 1 lists summarized information about risk levels for man, which was taken from the book by Ye. Ye. Kovalev [12].

Table 1. Risk of mortality and death of man under different conditions (per person per year)

| Conditions  | Level of risk                            |
|---|--|
| 1. Endogenous environment (mortality due to disease)  |  |
| all age groups  | $1 \cdot 10^{-2}$                        |
| 1-19 years  | $2.3 \cdot 10^{-2} - 3 \cdot 10^{-3}$    |
| 20-49 "   | $4 \cdot 10^{-4} - 4.8 \cdot 10^{-3}$    |
| 50-80 "   | $8.4 \cdot 10^{-3} - 14.3 \cdot 10^{-2}$ |
| 2. Exogenous environment  |  |
| smog, atmospheric pollutants, waste from nuclear electric power plants, medical treatment involving use of radiation, irradiation from television sets, radioactive fallout | $(3-6) \cdot 10^{-6}$                    |
| accidents (males)   |  |
| all ages  | $9.2 \cdot 10^{-4}$                      |
| 0-19 years  | $7.8 \cdot 10^{-4} - 7.2 \cdot 10^{-4}$  |
| 20-49 "   | $1 \cdot 10^{-3}$                        |
| 50-80 "   | $(1.2 \cdot 4.2) \cdot 10^{-3}$          |
| all types of vehicular accidents at 25-44 years of age (according to United States data)  | $1 \cdot 10^{-6} - 3.8 \cdot 10^{-4}$    |
| 3. Occupational activities  |  |
| industrial occupations (miner, builder, industrial worker)  | $1.2 \cdot 10^{-3} - 0.8 \cdot 10^{-4}$  |
| aviation  |  |
| civil aircraft crew   | $4.5 \cdot 10^{-4} - 0.8 \cdot 10^{-4}$  |
| crew of jet bomber  | $2.5 \cdot 10^{-3}$                      |
| fighter pilot   | $1.2 \cdot 10^{-2}$                      |
| pilot of series-produced jet fighter  | $2.0 \cdot 10^{-2}$                      |
| crew of military helicopter (maximum risk)  | $2.5 \cdot 10^{-2}$                      |
| nonindustrial occupations (fireman, steeple jack, tractor operator)   | $2 \cdot 10^{-4} - 8.5 \cdot 10^{-3}$    |
| occupational exposure to ionizing radiation (for 40 years in dosage of 1 rad/year)  | $1 \cdot 10^{-2}$                        |
| 4. Nonoccupational activities (sports)  | $3 \cdot 10^{-7} - 5 \cdot 10^{-4}$      |

The highest natural mortality (due to disease) level is observed in children and elderly people (over 14%). The mean indicator is 1% for all ages and 0.1% for those 25-40 years of age.

Ye. Ye. Kovalev [12] cites the following classification of risk levels for professional activity (% per year): safe--less than 0.01, relatively safe--0.01-0.1, dangerous--0.1-1 and particularly dangerous--over 1.

The first category is referable to such sectors of industry as shoe, textile, food and forestry and the last, to test pilots, crews of jet fighters and military helicopters. The question arises as to what risk level and for which category it should be acceptable and socially justified, in order to extrapolate on its basis the experimental data to man. Since the extrapolated value should ultimately be given for dosage or intensity of EMR for a specific risk level, the level of natural mortality could, of course, be the general indicator acceptable for animals and man. For man, one could also use an approach based on analysis of other than occupational accidents. As shown by analysis of all accidents from 1928 to 1972 (U. S. data), the risk level is about 0.05% per year. In the first approximation, this indicator can be considered a socially acceptable risk of death [12]. As stated above, the range of risk is 0.01-1%, i.e., there is 100-fold variation. This range is interesting in that one can cite on its basis the EMR risk for the public as 0.01%, for those working with EMR sources as 0.1 (tolerated dose) and 1% (justified risk dose). This conforms with the recommendations of ICRP for ionizing radiation, which proposes that one distinguish between only two categories: those working with radiation sources and the public. In the latter case, the dose levels should be one-tenth the value for the former. A decline of risk level in setting standards would inevitably lead to increased economic expenditures. The problem of "expenses-benefit" arises. Hypothetically, there could be such a situation that further reduction of harm from radiation would be economically and socially less advantageous. In other words, we could gain an inadequate advantage from lowering standards, as compared to economic expenses to provide protection and other medical and social measures. Such an approach has been developed in several works as applied to ionizing radiation [4, 12, 34]. Use of differentiated analysis of the "expenses-benefit" problem leads us to conclude that there is no validity whatsoever to the ideology of absolute safety, and it is socially unacceptable.

Society has not developed philosophical guidelines and methods for solving the problem of relationship between risk and benefit from using new equipment. At first glance, it appears quite humane and convenient to accept a new factor as being harmful or lower the level of its effect to such a value that the equipment generated by this factor becomes simply unrealistic. There may be negative consequences to society if it is deprived of the opportunity to use technological progress. While the harm to man (risk of disease, death) can be estimated quantitatively, it is sometimes quite difficult to assess the benefit, since it sometimes returns to an individual through public-social benefit, benefit to society as a whole.

Starr [45] graphically demonstrated that, in spite of the obvious increase in risk and harm to health, physical expenses and number of people using

the achievements of civilization are growing constantly (Figure 1). It should also be borne in mind that there is national benefit from a given product of human thought. This is particularly demonstrable in assessing the "harm-benefit" of nuclear electric power plants [42].

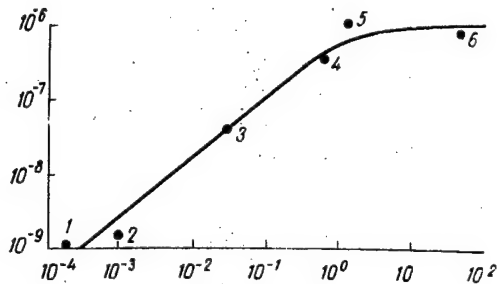


Figure 1.

Relationship between risk and benefit [45]. X-axis, indicator of benefit (benefit awareness), arbitrary parameter: social acceptability (awareness) of risk and related benefit or satisfaction, amount of monetary expenses, increase in number of people involved in a given risk category; y-axis, risk (in man-hours); risk of disease-- $10^{-6}$

- 1) atomic energy
- 2) army
- 3) railroad
- 4) smoking
- 5) civil aviation
- 6) motor vehicle

Evaluation of "threshold" levels of biological effect of EMR: At the present time, there are debates and doubts about the validity of different EMR standards. In the United States [44], there is sometimes criticism of  $10 \text{ mW/cm}^2$  energy-flux density (EFD) and opinions that this value is unjustified have been voiced. In the USSR, the existing standards have been updated, and the most recent GOST [All-Union State Standard] raised from 10 to  $25 \mu\text{W/cm}^2$  the standard of exposure to microwave radiation for an 8-h work day.

The first suggestion of  $10 \text{ mW/cm}^2$  as the permissible level of microwave irradiation was made by H. Schwann [43] in 1953. S. Michaelson [38] provided comprehensive physiological and biophysical validation of the policy for standardization of EMR in the United States. The American National Institute of Standards (ANIS) recommended it as the basic standard. More rigid standards (lower by a factor of  $10^3$  than the American ones) was proposed by the laboratory of Z. V. Gordon [5] and they were recommended as safe levels in 1958. The methodology

for validating these standards was the exact opposite, and this was the subject of lengthy debates among scientists.

Analysis of the literature reveals a distinction: some researchers in such countries as Sweden, Italy and France generally tend to hold a more rigid position than the United States with respect to biological significance of EMR. These countries decided to obtain their own data on standardization of this factor, since they did not trust the leading countries that had studied the biological effects of EMR for a long time.

Introduction of any standard is a lengthy and painful process, particularly in the case of safety standards for the effect of some factor on man. Thus, work on U. S. standard C95.1-1966 for microwave radiation began as far back as 1942. Even when it was set (1960's), there was no agreement among scientists. Some private companies (such as Bell Telephone and General Electric) introduced

a more rigid standard, 1 and even 0.1 mW/cm<sup>2</sup>. The U. S. standard was finally approved in 1966. However, this was only the beginning of further discussion of the problem, and immediately the question arose about the standard for nonoccupational exposure to microwaves [46].

The wide distribution of EMR sources attracted the attention of prominent specialists in the field of ionizing radiation of the International Association for Radiological Protection. Since 1973, the problem of nonionizing radiation began to be considered within the limits of the ICRP. If standardization of nonionizing radiation were done in the same way as for ionizing radiation there would not be such significant differences between the allowable EMR values in different countries.

Without going into the debatable aspects of specific and nonspecific effects of EMR, for the purpose of setting standards one should recognize only the specificity of distribution of absorbed energy. At the present stage of our knowledge about the biological effects of EMR, one can discuss with sufficient certainty only the thermal effect of EMR, referring here also to the possible absence of elevation of body temperature. The latest studies on EMR dosimetry have contributed many interesting elements to the problem of standard setting.

In validating the allowable doses of EMR, the following should be viewed as the basic factors: biophysical and pathophysiological distinctions of action; quality of radiation (frequency, modulation); irradiation conditions (non-uniform, orientation of object in field, grounding); recovery and residual effects; targets of standardization (public, occupational activity); ratio between benefit and harm of the factor for which a standard is being set.

Our interpretation of the basic methodological guidelines for setting hygienic standards of EMR is essentially similar to those described by B. M. Savin, A. G. Subbota and B. A. Chukhlovin [16, 17, 20].

However, only mortality, reduction of life span, malignant neoplasms, cataract and genetic effects can be considered unconditionally reliable criteria. It is difficult to prove deleteriousness according to other criteria.

We wished to call attention to the following aspect of setting standards for EMR. At a specific intensity of this factor there may be electric discharges, detonation, etc. [37]. When special work clothes become charged with electricity in an area where there is a high danger of fire, it could lead to an accident. For this reason, the medical standards must definitely be lower than the "safe" EMR level for equipment.

As in the case of ionizing radiation, the biological effects of EMR can be analyzed according to such criteria as cataract, changes in gonads, life span and lethal effects. All these factors can be evaluated in a strictly quantitative manner, although their significance is apparently different.

In assessing the effect of ionizing radiation on the public, genetic effects are the principal ones; however, in assessing the biological effectiveness of EMR we rank them in last place. Reliable facts have not been obtained for this

parameter, although it is possible to do so in theory, since thermal effects in experiments on the *Drosophila* fly were mutagenic. It is difficult to make a quantitative estimate of the effects of EMR on the central nervous system [3].

We discussed above the risk factor as a criterion in setting standards for deleterious environmental effects and there was validation of a value of 0.1%, which was taken as the minimum level of occupational risk and 1/10th of this value for the public. One can use other ratios that were adopted in setting standards for ionizing radiation, where the standard for occupational exposure [7, 14] was taken as the reference point (as 1). Normalizing for the risk level, we shall obtain 0.003 (for the entire population), 0.01 (for the public close to sources) and 0.1 (occupational exposure). Thus, the main task is to set the standard dose and intensity of EMR for "professionals."

American standards are based on using the thermal effect as a criterion of EMR. The philosophy of this approach has been described in detail in several works [26, 31-33, 38, 40, 43, 47]. The methodology and validation of standards in our country, as well as the Polish People's Republic and CSSR, are well-known [5, 16, 17, 20, 25, 36, 41]. They are based primarily on pathophysiological changes in the central nervous system, cardiovascular and hemopoietic systems, as well as hygienic observations in industry.

Apparently, the standards for "professionals" should be based on less rigid medical approaches than for the public, with consideration of ergonomic and economic aspects. For this reason, the range of EMR dose levels must be more diversified: critical dose, dose of justified risk and tolerated dose. Occupations involving high psychophysiological tension, in which a slight loss of efficiency in performing functional duties could lead to an accident, require a special approach with regard to setting standards.

One can follow three routes to obtain standards for man exposed to EMR: 1) considering the similarity of thermal stress in all warm-blooded creatures, including man, and absence of specificity of different thermal factors, one determines the safe levels of thermal effect of EMR; 2) demonstration of some significant effect of low-intensity (proposed threshold values) EMR in animals and its extension to man with a certain share of probability; 3) extrapolation to man of experimental data (on the level of accepted risk) obtained in the range of high-intensity EMR, which elicit very definite and reliable effects, to the extent of animal death; proof that the effect is a stochastic function of dosage.

The first and rather wise suggestion based on thermal balance of man was made by H. Schwann [43]. Under normal conditions, the human body can eliminate heat into the environment (on the order of  $10 \text{ mW/cm}^2$ ). This corresponds to man's energy expenditure during light work. Under certain favorable conditions, this could reach  $100 \text{ mW/cm}^2$ . The American National Institute of Standards introduced  $10 \text{ mW/cm}^2$  as the basic value [43]. The rather comprehensive work of R. Tell and F. Harlen [47] deals with proof of this value from the standpoint of man's thermal balance with exposure to EMR. Lack of

rise in endogenous temperature of more than 1°C is considered as an additional criterion. At the present time, the standards of the United States, England, FRG and Canada are differentiated according to radiation frequency [26, 32, 33].

The results of analysis of data in the literature [3, 10, 24, 27, 39, 47] concerning the biological effects of EMR can be formulated in the form of the following conclusions and theses, which reflect our opinion.\*

In the case of total-body exposure to microwaves, the occurring changes in physiological functions are a reflection of thermal stress, as in the case of infrared radiation.

Stressor manifestations occur with an additional thermal burden, which is close to the value of basal metabolism (about 10 W/kg for mice, 5 for rats and about 2 for dogs); a 2-fold or greater increase in thermal burden of EMR, as compared to basal metabolism, leads to marked physiological changes in the case of long-term exposure.

Changes in rectal temperature and temperature in the region of the hypothalamus can be recorded with 20-30% change in basal metabolism; approximately 10% is the bottom limit of fluctuation of basal metabolism.

There are very distinct dose-effect functions, which can be analyzed by the methods used in radiobiology of ionizing radiation.

One should make a strict distinction between the different effects caused by high EFD with short exposure time and low EFD with long-term irradiation; in the former case, the specifics of EMR are distinctly demonstrable by the thermal distribution of absorbed energy in the body.

Thermal modeling of EMR has limited application and it "works" only at an intensity equal to or greater than basal metabolism, when heat regulation is effected mainly by such parameters of a biological system as surface and mass of the body.

Most biological effects of EMR are valid only for the region of the formed wave; in view of the difficulty of dosimetric evaluation of absorbed dose in the near zone, it is difficult to predict some biological effects.

The small number of observations pertaining to "mild effects" require further investigation; use of 10 as the reserve coefficient takes into consideration, to some extent, any possible, unpredictable effects.

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\*Some of the theses are hypothetical.

Determination of different categories of tolerated doses of EMR effects on man was based on the following assumptions:

- 1) The main biological effects demonstrated in animals are also inherent, to some extent or other, in man.
- 2) At certain EFD levels, death may also occur in man. Death as a function of dose will also be governed by stochastic rules.
- 3) The death effect corresponds to the level of heat accumulation and body temperature (rectal temperature may serve to reflect it).
- 4) The "threshold" effect of EMR can be determined according to the criterion of risk of death; the level of undeterminate death is taken as 0.1% and the range of risk levels for man is 0.01-1%.
- 5) After exposure to EMR, recovery is very rapid, while cumulative effects play an insignificant part in the case of long-term exposure; the rate of recovery and magnitude of accumulation are estimated strictly quantitatively.
- 6) Heat accumulation in the body in the case of long-term exposure at the level of 0.01-0.1% death rate can be an analogue of absorbed dose; effective dosage is estimated by the biological effectiveness of absorbed dose; at high EFD the effective dose is virtually the same as the absorbed dose.
- 7) When dose rate is increased and accumulated dose is constant, local effects of EMR acquire increasing significance, and in the case of maximum possible accumulated dose and exposure time of less than 5 min (brain circulation time) the general thermal models may not "work" due to the "false" triggering of heat-regulation centers.
- 8) Appearance of local "hot spots" at certain frequencies is a special instance of total-body uncontrolled irradiation, and introduction of the reserve coefficient in setting standards smoothes out the vagueness of biological effect of EMR.
- 9) The methodology of extrapolating experimental data to man should not differ basically from the one used in radiobiology of ionizing radiation.
- 10) There should be two gradations for obtained values of tolerated doses: for "professionals" (controlled irradiation conditions) and for the public (irradiation conditions are relatively difficult to control).

11) The risk from EMR for "professionals" should not be lower than the lowest risk level for man referable to other factors and higher than with exposure to ionizing radiation for 40 years in a dosage of 1 rad/year.

12) The risk to the public must be at least 1/10th the lowest allowable level for professionals.

Extrapolation to man of experimental data on dose and time characteristics of microwave radiation: We submit here some views on extrapolation of experimental data to man for a death criterion of 0.1% frequencies of 2-3 GHz. Experimental data have been reported [3, 9, 10] and the corresponding ratios between EFD and dose (time) of irradiation; determination was made of thresholds of intensity, which constituted 25 mW/cm<sup>2</sup> at t>60 min for mice, 40 for rats and 80 for dogs. At t<60 min, EFD is a logarithmic function of radiation dose. The coefficient of regression constituted 0.7 for all species studied.

Table 2 lists some physiological characteristics for different animals that are closely related to thermal homeostasis. Body mass was taken as the main correlated parameter.

Table 2. Main physiological parameters of man, dog, rat and mouse and their comparison to threshold EFD values

| Physiological parameter   | Man          | Dog  | Rat   | Mouse |
|---|--------------|------|-------|-------|
| Body weight, kg   | 70           | 11   | 0,25  | 0,025 |
| Body surface, m <sup>2</sup>  | 1,8          | 0,44 | 0,045 | 0,006 |
| Pulse rate, per min   | 70           | 110  | 400   | 500   |
| Respiration rate, per min   | 16           | 20   | 120   | 175   |
| Pulmonary ventilation, cm <sup>3</sup> /(g·min)                     | 0,13         | 0,19 | 0,65  | 1,24  |
| Fluid metabolism half-life, days                                    | 10           | 5    | 2,5   | 1,6   |
| Oxygen uptake, l/(kg·h)   | 0,21         | 0,33 | 0,87  | 1,65  |
| Basal metabolism, mW/cm <sup>2</sup>                                | 4,56         | 4,60 | 3,13  | 3,83  |
| " " mW/g  | 1,17         | 1,84 | 4,85  | 9,20  |
| EFD eliciting no more than 0.1% death (2.4 GHz): mW/cm <sup>2</sup> | 120 (125)*80 | 80   | 40    | 25    |
| mW/g  | 4-5          | 3,2  | 8     | 18    |

Note:  $V_g = 53.5 \cdot M^{-0.26}$ ;  $V_c = 241 \cdot M^{-0.25}$ ;  $V_{O_2} = 0.675 \cdot M^{-0.25}$ , where  $V_g$ ,  $V_c$ ,  $V_{O_2}$  and  $M$  are respiration rate (per min), pulse rate (per min), oxygen uptake [l/(kg·h)] and body mass (kg), respectively. Asterisk shows extrapolation for body mass:  $I = 14 \cdot M^{0.19}$ ; in parentheses--for body surface:  $I = 9 \cdot S^{0.27}$ , where  $I$  is EFD (in mW/cm<sup>2</sup>);  $S$  is body surface, cm<sup>2</sup>.

As can be seen in Table 2, such parameters as body surface, basal metabolism, pulse rate and respiration rate, pulmonary ventilation, fluid turnover half-life and oxygen uptake are correlated with body mass. There is an inverse relationship between body mass and these parameters with a regression coefficient of 0.25. Even in trees, there is a link between oxygen uptake and

mass and the slope in the curve is similar to that of warm-blooded animals. This relationship in such diverse species of animals and plants enables us to view this as a general biological phenomenon [23]. For threshold values (risk level of 0.1%), EFD correlates well with body mass or surface ( $r = 0.99$ ) (Figure 2). The extrapolated value of EFD for man constituted 120-125 mW/cm<sup>2</sup>

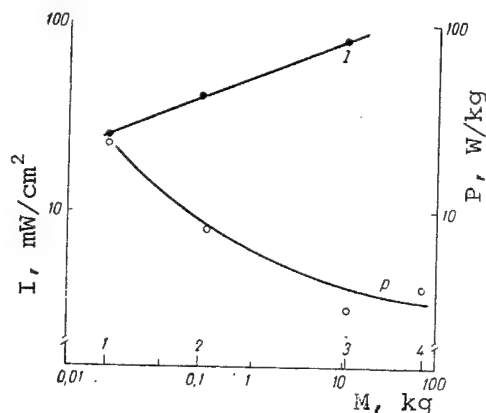


Figure 2.

Relationship between incident (1) and absorbed (P) threshold dose at frequency of 2.4 GHz as a function of body mass (free space without consideration of reflecting surfaces)

- |              |        |
|--------------|--------|
| M) body mass | 2) rat |
| I) EFD       | 3) dog |
| P) SAE       | 4) man |
| 1) mouse     |        |

Extrapolated values for man:

$I = 126 \text{ mW/cm}^2$ ,  $P = 3.6 \text{ W/kg}$

(Table 2). Thus, 4 W/kg can be considered the threshold value of specific absorbed energy (SAE) for man exposed to radiation for a long time. Assuming that there is an analogous function of exposure time at EFD of more than 100 mW/cm<sup>2</sup>, we shall obtain:

$$\log I = 3.25 - 0.7 \log t \quad (f \geq 2 \text{ GHz}) \quad (1)$$

where  $I$  is EFD (in mW/cm<sup>2</sup>) and  $t$  is irradiation time (min).

If we consider that the reserve coefficient equals 10, it will overlap the extreme values of SAE at frequencies of 10 MHz - 10 GHz (0.04-0.2) and lower the risk to 0.01%. Then equation (1) would acquire the following appearance:

$$\log I = 2.25 - 0.7 \log t \quad (5 \leq t < 60) \quad (2)$$

The range in which the formula "works" is: 5 min--circulatory cycle in the brain; 60 min--exposure time with which EFD is 10 mW/cm<sup>2</sup> ( $f = 2.4 \text{ GHz}$ ) or 0.4 W/kg.

Figure 3 illustrates exposure time as a function of EFD and SAE for resonance (30-300 MHz) and the other (>300 MHz) frequencies. To convert EFD to SAE, we used coefficients of 0.04-0.2 [30]. Even under resonance conditions with 10 mW/cm<sup>2</sup>, SAE was only 2 W/kg, which corresponds to energy expended with moderate physical exercise. Under uncontrollable exposure conditions, one must bear in mind that the resonance range of frequencies constitutes about 0.02% of the total radiofrequency range (0.001-300 GHz). We obtained a threshold value of 1 mW/cm<sup>2</sup> for the public. At 2-3 GHz, SAE is 0.04 W/kg and with resonance 0.2 W/kg, which does not exceed the usual physiological fluctuation of basal metabolism. One can consider 2 W/kg (50 mW/cm<sup>2</sup>,  $f = 2.4 \text{ GHz}$ ) with no more than 5 min exposure time as the warranted risk dose under strictly controlled conditions (absence of grounding or reflective surfaces).

Animal death occurs as a result of thermal overheating with rectal temperature increment ( $\Delta T$ ) of more than 2°C [21].  $\Delta T$  increment of 6°C elicits death of all species of animals [23]. For dogs, EFD (in mW/cm<sup>2</sup>) as a function of

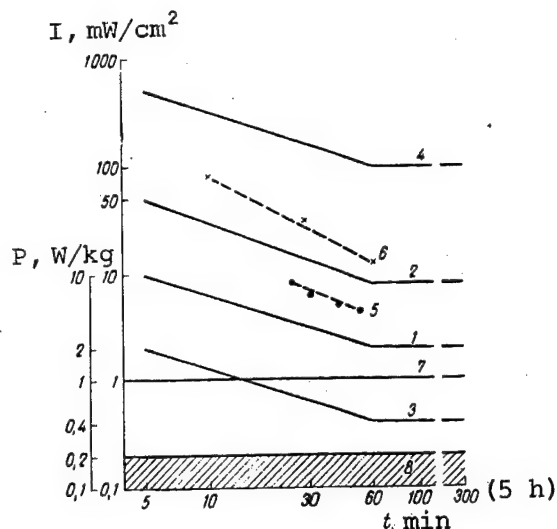


Figure 3.

Threshold values of EFD (1) and SAE (P) for man as a function of exposure time ( $t$ ) in the case of free space without reflective surfaces

Professionals:

- 1) tolerated EFD for frequencies of 30-300 MHz (resonance conditions)
- 2) tolerated EFD for other frequencies
- 3) tolerated SAE
- 4) critical EFD (without reserve coefficient for 0.1% risk) for nonresonance frequencies (obtained by extrapolation of experimental data to man)
- 5) data of Blokli (see [1]) on human tolerance to thermal load during exercise
- 6)  $1^\circ\text{C}$  rise in body temperature as a function of EFD and EMR exposure time at frequency of 2.45 GHz (extrapolated data)

Public:

- 7-8) maximum EFD and SAE, respectively, under any exposure conditions

man, the distribution of energy will be analogous only at a frequency of about 350 MHz. The established correlation between impaired heat balance and such a biological act as death is indicative of the thermal nature of

exposure time (seconds) was obtained experimentally, and it has the following appearance for  $T = 2.5^\circ\text{C}$  (0.1% death):

$$I \cdot t = 130 \text{ (J/cm}^2\text{)} (f=2.45 \text{ GHz}) \quad (3)$$

A comparison of EMR intensities obtained from this function and the equation,  $\log I = 3.15 - 0.82 \log t$  [10] shows that they coincide well, which entitles us to consider heat accumulation as an analogue, to some extent, of absorbed dose. For man, a heat increment of about  $0.5^\circ\text{C}/(\text{J} \cdot \text{g})$  was obtained. Justesen [35] cites  $0.25^\circ\text{C}/(\text{J/g})$ . The differences could be related to dose rate.

Several values (as an example) of EFD are plotted in Figure 3 for  $\Delta T = 1^\circ\text{C}$ . All of the points are above the tolerance curve calculated for an 0.01% death criterion.

If we were to normalize the curve of EMR tolerance for nonresonance conditions (see Figure 3, curve 1) for the corresponding value of  $\Delta T^\circ\text{C}$ , we would see that it reflects an  $0.3^\circ\text{C}$  elevation of body temperature. Calculation of  $T$  using equations of heat accumulation during exposure to EMR [10, 22, 47] shows a good coincidence. With exposure time of 5-60 min and EFD 58-10  $\text{mW/cm}^2$ ,  $\Delta T$  constituted about  $0.1-0.2^\circ\text{C}$ . In assessing the "threshold" values of EFD using the criterion of impaired behavioral reactions of 3 animal species--rats, squirrel monkeys and Macaca rhesus--Delorge [29] obtained an extrapolated value of EFD for man on the order of  $100 \text{ mW/cm}^2$  (correlation with body mass) at a frequency of 2.0 GHz.

Extrapolation for such a criterion as death makes it possible to avoid such an objection: distribution of electromagnetic energy at 2.45 GHz is different in mice than in dogs, let alone man. In

electromagnetic effects of total-body exposure to less than  $100 \text{ mW/cm}^2$ . A  $1^\circ\text{C}$  elevation of  $\Delta T$  can be expected with a thermal load that is 1.5-2 times greater than basal metabolism. This is consistent with the estimates of R. Tell and F. Harlen [47]. Metabolic heat resulting from physical exercise and heat generated by EMR (80 MHz) equals  $170 \text{ W}$  ( $\sim 2.5 \text{ W/kg}$ ) elicits a  $1^\circ\text{C}$  elevation in temperature of the hypothalamus [47]. In approximately 1 h, the heat burden was  $8 \text{ J/g}$ , which is close to the value of  $7.2 \text{ J/g}$ , which we obtained.

Thus, an additional electromagnetic burden must be related to ambient temperature conditions and physical exercise. Accumulated heat must not exceed a certain critical level.  $\Delta T$ , metabolic rate or heart rate can serve as such criteria. Most researchers cite  $39\text{--}39.5^\circ\text{C}$  body temperature, pulse rate of  $120\text{--}140/\text{min}$  at rest, body temperature of  $40\text{--}40.5^\circ\text{C}$  and pulse rate of  $160\text{--}180/\text{min}$  during physical work as the maximums. The WHO Committee of Experts discussed recommendations to the effect that a pulse rate of  $160/\text{min}$  and body temperature of  $38\text{--}39^\circ\text{C}$  be considered the maximum [1].

Most researchers believe that the same physiological state occurs regardless of how heat accumulates--under the effect of an external burden, provided there is inadequate heat transfer or due to accumulation of metabolic heat. Roth and (Blok) [1] defined the following limits for accumulation of metabolic heat due to physical loads:  $293 \text{ W}$  ( $4.2 \text{ W/kg}$ )--47 min,  $439 \text{ W}$  ( $6.3 \text{ W/kg}$ )--38 min,  $579 \text{ W}$  ( $8.3 \text{ W/kg}$ )--30 min--and  $725 \text{ W}$  ( $10.4 \text{ W/kg}$ )--24.5 min. Temperature in the auditory meatus rose to  $39.7^\circ\text{C}$  and pulse rate reached  $180/\text{min}$ . Of course, it is hardly expedient to be governed by these figures, but they are of interest as maximum thermal homeostasis in man. As compared to basal metabolism, maximum energy expenditures could increase by more than 10 times, to  $15 \text{ mW/cm}^2$  or more. Infrared irradiation in a dosage of  $28\text{--}56 \text{ mW/cm}^2$  is tolerated for a long time, and there is no associated pain. The latter was observed only at  $105 \text{ mW/cm}^2$ .

The most suitable criterion of EMR tolerance (according to thermal effect) can also be considered the accumulation of metabolic heat during exercise. A value of  $4 \text{ W/kg}$  can be accepted as the critical level, which corresponds to EFD of  $100 \text{ mW/cm}^2$  ( $2.45 \text{ GHz}$ ) and  $0.1\%$  risk.

It is difficult to go from absorbed to effective dose primarily due to two circumstances: high rate of recovery (as applied to thermal stress--elimination of heat) and absence of strictly reliable figures for residual irreversible damage in the case of long-term electromagnetic irradiation.

The first thesis has been proven experimentally; as for the second one, there are grounds (also experimental) to assume that there is an irreversible component. However, it has not yet been quantitatively defined. For this reason, there are two possible routes for assessing the recovery period in man: experimental with subsequent extrapolation to man, and search for information in the literature concerning elimination of thermal stress in the case of ordinary overheating.

In the first case, there are data [9] concerning estimation of recovery period (death criterion) which constituted about 8 min of EFD  $800 \text{ mW/cm}^2$

(12 J/cm<sup>2</sup>) for mice. In the case of repeated exposure with this EFD and an interval of 10 min, the overall accumulated dose reached 2210 J/cm<sup>2</sup> (88 J/g). There were no cases of animal death. Consequently, the time for total recovery constitutes no more than 10 min for mice and rats. The recovery period was estimated at 30 min for dogs (elimination of heat according to change in  $\Delta T$ ), 22 min for respiration rate and 70 min for pulse rate [21]. All these values were obtained with critical exposure to EMR, when  $\Delta T$  reached 2-3°C. By extrapolating the recovery period from animals to man (correlation with body surface), we shall obtain 50 min as total recovery time. The recovery time for heart rate will increase proportionately to 120-140 min. All these values can be expected with  $\Delta T = 2-3^\circ\text{C}$ . At  $\Delta T = 1^\circ\text{C}$ , recovery time for temperature homeostasis will decrease to 30 min, i.e., to one-half [11]. At the  $\Delta T$  values, for which tolerated exposure levels were standardized, the recovery period for body temperature and respiration rate would not exceed 15 min and for pulse rate, 30 min. Of course, this parameter should be used only with SAE in excess of 1 mW/g. Under actual conditions, the rate of recovery of human thermal balance could be even higher. Thus, heat transfer of the skin could increase by 10 times, from 0.7 to 6 mW/cm<sup>2</sup>. With SAE of 2 mW/g, it is assumed that there is a thermal equilibrium in man under comfortable ambient conditions at complete physical rest. Thus, estimation of effective dose is acceptable in the case of multiple exposure to divided doses of radiation delivered at a dose rate of more than 1 mW/g and in a dosage of more than 3 J/g.

The residual effect (irreversible component by analogy to ionizing radiation) is not demonstrable by  $\Delta T$ . Nor is it demonstrated by the death criterion from single exposure to electromagnetic waves. Moreover, it is not demonstrable in the case of combined exposure to ionizing radiation and EMR with SAE of 10 W/kg (experiments on mice). It is only at 40 W/kg or more that residual damage is demonstrable by this method. However, as soon as we turn to evaluation of different systems in the case of chronic exposure to EMR (hemopoiesis, endocrine and teratogenic effects), some changes are demonstrable with EFD on the order of 2 W/kg or more. It would be unwise to exclude the numerous observations under industrial conditions, which confirm the phenomenon of irreversible component of damage. However, it is not deemed possible as yet to cite a definite figure in joules for residual damage. We can only make the following assumptions. On the basis of experimental data on the combined effect of nonionizing radiation and EMR for dose rates in excess of 2 mW/g and doses over 7 J/g, the maximum residual damage will not exceed 1%. At less than 2 mW/g and 7 J/g it becomes negligibly small. The complexity of local distribution of EMR energy in the human body does not allow us to entirely exclude residual damage. One should pay attention to local SAE in the region of the head, neck, eyes and testes. Cataract, genetic and teratogenic effects are difficult to extrapolate to man. It is difficult to assume, for example, that a cataract would be caused in man at higher EFD than in experiments on rabbits.

One must also take into consideration the effect of reflective surfaces (possible 25-fold increase in SAE), grounding (2-8-fold increase in SAE), polarization, local SAE that could be 10 times higher than mean SAE. Dosimetry in the near zone also contributes much uncertainty. Such factors as physical

load and ionizing radiation could raise SAE to rather high values (for example, ionizing radiation, by 1.5-2 times) [10]. All these factors can be taken into consideration for protection purposes only under strictly controlled conditions, which are inherent in industry, for medical use and, of course, in experiments. It is expedient to introduce the concept of coefficient of quality, which enables us to estimate approximately averaged SAE or effective EFD under real conditions. Thus, standardization of EMR for man cannot be based solely on extrapolation of experimental data obtained for other species. A number of questions can be investigated only on man. The well-known geneticist, V. Makkyusik [13] observes that "man himself is the best subject for studying man." For this reason, only epidemiological studies can be the last and undisputed judge of any hygienic standards. Only they give us the right to discuss the harm or harmlessness of some factor or other. The difficulty of epidemiological investigations of EMR is that it has no specific or even distinct clinical symptoms. Moreover, in real life, EMR is always associated with other, even more significant factors, for example, ionizing radiation. And in this sense, the general guidelines for setting standards are intertwined, to some extent, with the general guidelines for biological evaluation of the combined effect of factors in the industrial environment. It is very difficult to select criteria for epidemiological survey of a group of people in contact with EMR. Evidently, the most suitable criteria in this case will be primarily morbidity (particularly blood diseases), aging ("index of old age," which is used extensively by Japanese and American researchers), reproduction and genetic effects. In particular, the aging phenomenon can, in our opinion, be evaluated indirectly according to increase in risk of death due to accidents. Evaluation of the effect of EMR on man's efficiency as an operator is a rather important criterion. This is a particularly difficult question.

There is a reverse side to any discussion on setting hygienic standards for any factor: the social response is not necessarily adequate, and this causes hyperbolization of danger. This inevitably affects technological progress. It is always more difficult to convince social awareness of the national benefit of some factor or other. But, to avoid the other extreme, EMR standards must be very validated. It would be desirable in this area of human endeavor for there to be the same situation as in the atomic industry, where the risk level is lower by many orders of magnitude than in other sectors of industry.

In conclusion, it should be noted that the "threshold" levels of electromagnetic fields we have discussed by no means presume to be standards. Rather, they are a pretext for a discussion. We are fully aware of the complexity of the problem and its contradiction. And, as is clearly evident from the decision adopted by the All-Union Symposium on Biological Effects of Electromagnetic Fields [2], there are more unanswered questions here than solved problems.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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FLUID-ELECTROLYTE METABOLISM AND RENAL FUNCTION IN COSMONAUTS FOLLOWING  
185-DAY SPACEFLIGHT

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[Article by A. I. Grigor'yev, B. R. Dorokhova, V. Yu. Semenov, B. V. Morukov,  
E. O. Baychorov (deceased), I. S. Skukina and B. V. Afonin]

[English abstract from source] Fluid-electrolyte metabolism and renal function of the crewmembers of the 185-day spaceflight were examined. Various changes in fluid-electrolyte metabolism and its regulation were seen in the Commander and Flight Engineer. As most other crewmembers who performed similar flights, Cr showed fluid and sodium retention, whereas FE displayed higher than pre-flight sodium excretion in the urine. These differences were associated with individual variations of regional hemodynamics which modified the renin-angiotensin-aldosterone system in a different manner. Postflight both crewmembers showed a higher excretion of bivalent ions. The higher excretion of calcium was accompanied by a lower concentration of total and ionized calcium in the serum as well as by a lower concentration of PTH and calcitonin. The loading KCl test made it possible to assess variations in potassium metabolism that occurred during flight. They included the inability of tissues to retain potassium due to atrophic processes which developed in the weightless state and due to the unloading of the musculo-skeletal system.

[Text] Man's exposure to spaceflight factors (SF) leads to functional changes in virtually all systems of the body [3, 7, 10]. Determination of the causes and mechanisms of observed changes is one of the basic tasks of space medicine. Alteration of fluid-electrolyte metabolism (FEM) plays an important part in man's adaptation to SF [4, 14]. The data available at the present time are indicative of dependence of the nature of FEM changes on duration of exposure to SF [5, 11]. For this reason, it was deemed important to study renal function, FEM and systems of their regulation following long-term spaceflights.

Methods

We examined FEM and renal function several times preflight and for 12 days after flight in the crew of Salyut-6 orbital station who had been on a 185-day mission.

We assessed FEM according to blood and urine levels of sodium and potassium (flame photometry), total calcium (titrometry), ionized blood calcium (direct potentiometry using an ion-selective electrode), magnesium (atomic absorption spectrophotometry), creatinine (spectrophotometry for Jaffe's reaction with picric acid). In addition we measured in blood serum the concentration of C-fragment of parathyroid hormone (PTH) and calcitonin (CT). Aldosterone concentration was assayed in blood and urine. Renin activity was measured in blood plasma. Samples were counted on a 1285 gamma counter (Tracor) and Mark III beta counter (Tracor). We performed the potassium-fluid load test before the spaceflight and on L+2 to assess ion-regulating function of the kidneys [1].

All of the studies were conducted while keeping records of fluid and salt intake. We used both absolute values for excretion of fluid and ions, and their percentile excretion (in relation to intake) [8].

### Results and Discussion

On the 1st postflight day, the commander (CDR) presented a decline in serum potassium concentration (3.4 meq/l versus 3.9 meq/l before the spaceflight) and in the flight engineer (FLE) there was merely a tendency toward decline in concentration of this ion (4.0 meq/l versus 4.2 meq/l before the flight). On the 7th postflight day, CDR showed a tendency toward increase in concentration of potassium, but it did not reach the base level (3.7 meq/l). In the FLE, blood potassium level did not differ from pre-flight values (4.15 meq/l). Blood sodium levels changed insignificantly in both cosmonauts. At the same time, excretion of both ions in urine differed from preflight levels.

On L+0, the rate of excretion of fluid in the urine fraction collected immediately after landing from both cosmonauts showed virtually no difference from the base rate, which could be due to intake of a fluid and salt supplement at the last stage of the spaceflight [4]. In the next urine fraction collected during the night, the rate of fluid excretion, as well as sodium and potassium, was lower (Table 1). Fluid elimination was high on all other tested days.

At the same time, urine concentration of sodium decreased on L+1 and reached lowest values in the morning batch of urine in the CDR (see Table 1). As a result, there was decrease in both rate of excretion of this ion and its elimination in 24 h. However, already on L+3, concentration and rate of excretion of sodium did not differ from preflight findings. It should be noted that the changes demonstrated for the first 2 days were not due to a low sodium content in the food allowance (Table 2), but to replacement of its shortage, which developed in weightlessness.

In the FLE, on the 1st day of the postflight examination there was a high concentration of sodium in urine which, against the background of high rate of fluid excretion, caused more to be eliminated in both absolute figures and in relation to intake (see Table 2).

Table 1. Elimination of fluid (ml/min), concentration (I, meq/l) and rate of excretion of electrolytes (II,  $\mu$ eq/min) on L+0 and L+1

| Time of examination | Diuresis | Sodium |    | Potassium |    | Na/K |
|---------------------|----------|--------|----|-----------|----|------|
|                     |          | I      | II | I         | II |      |

|                     |           |        |        |        |        |     |
|---------------------|-----------|--------|--------|--------|--------|-----|
| CDR                 |           |        |        |        |        |     |
| Before spaceflight: |           |        |        |        |        |     |
| morning batch       | 0,63±0,04 | 201±12 | 127±8  | 49±3,2 | 31±3,8 | 4,0 |
| mean per 24 h       | 0,69±0,06 | 183±15 | 126±11 | 57±4,0 | 39±2,9 | 3,0 |
| After spaceflight:  |           |        |        |        |        |     |
| L+0                 |           |        |        |        |        |     |
| 11 Oct 6:45 pm      | 1,17      | 88     | 103    | 64     | 74,9   | 1,2 |
| 12 Oct 11:10 am     | 0,32      | 77     | 24,6   | 69     | 22,1   | 1,1 |
| average per 24 h    | 0,75      | 83     | 64     | 67     | 49     | 1,2 |
| L+1                 |           |        |        |        |        |     |
| 12 Oct 6 pm         | 0,37      | 56     | 20,7   | 71     | 26,3   | 0,7 |
| 12 Oct 10 pm        | 0,83      | 38     | 31,5   | 47     | 39,0   | 0,8 |
| 13 Oct 2 am         | 1,60      | 16     | 25,6   | 14     | 22,4   | 1,1 |
| 13 Oct 12:05 pm     | 0,79      | 10     | 7,9    | 30     | 23,7   | 0,3 |
| average per 24 h    | 0,90      | 30     | 21,4   | 40     | 27,9   | 0,7 |

|                     |           |        |        |        |        |     |
|---------------------|-----------|--------|--------|--------|--------|-----|
| FLE                 |           |        |        |        |        |     |
| Before spaceflight: |           |        |        |        |        |     |
| morning batch       | 0,42±0,10 | 239±23 | 99±21  | 65±6,9 | 26±2,8 | 3,0 |
| mean per 24 h       | 0,60±0,59 | 184±17 | 127±14 | 82±9,6 | 57±6,0 | 2,0 |
| After spaceflight:  |           |        |        |        |        |     |
| L+0                 |           |        |        |        |        |     |
| 11 Oct 1 pm         | 0,54      | 127    | 69     | 75     | 41     | 1,7 |
| 12 Oct 11 am        | 0,34      | 117    | 40     | 78     | 27     | 1,5 |
| average per 24 h    | 0,44      | 122    | 54     | 77     | 34     | 1,6 |
| L+1                 |           |        |        |        |        |     |
| 12 Oct 3 pm         | 0,63      | 120    | 76     | 74     | 49     | 1,7 |
| 12 Oct 11 pm        | 0,90      | 250    | 225    | 78     | 66     | 3,4 |
| 13 Oct 4 am         | 1,60      | 212    | 340    | 27     | 43     | 7,8 |
| 13 Oct 12:05 pm     | 0,97      | 206    | 200    | 25     | 25     | 4,0 |
| average per 24 h    | 1,00      | 197    | 210    | 50     | 44     | 3,9 |

Considering that the changes in sodium metabolism were more marked in the CDR than that of potassium for the first 2 postflight days, the Na/K ratio declined and reached lowest values during the night of L+1 (see Tables 1 and 2). In the FLE, Na/K was higher than the preflight value (see Table 1). These findings enable us to indirectly assess change in activity of mineralocorticoids.

There have been repeated reports [2, 12] previously about increase in mineralocorticoid activity following flights of shorter duration. Indeed, blood aldosterone concentration increased postflight in the CDR, which could have been the deciding factor in increasing distal reabsorption of sodium, perhaps in exchange for potassium [13]. Moreover, this cosmonaut presented a 25% increase in plasma renin activity, which could have an effect on sodium reabsorption, both directly and through change in renal blood flow [9]. Evidently, the demonstrated changes in hormonal regulation were attributable chiefly to the effect of earth's gravity, they were primary and caused changes in sodium and potassium excretion in urine. Analogous findings were made after ground-based studies with antiorthostatic hypokinesia [head-down tilt] of analogous duration [6].

Table 2. Excretion in urine (I) and intake (II) of electrolytes (in meq) and fluid (ml) before and on 2d-12th days after spaceflight

| Time of examination       | Fluid   | Sodium |     | Potassium |     | Calcium  |    | Magnesium |    |
|---------------------------|---------|--------|-----|-----------|-----|----------|----|-----------|----|
|                           |         | I      | II  | I         | II  | I        | II | I         | II |
| CDR                       |         |        |     |           |     |          |    |           |    |
| Before spaceflight (n=18) | 990±51  | 181±12 | 225 | 56±6      | 88  | 8,8±0,9  | 62 | 4,6±0,5   | 37 |
| After:                    |         |        |     |           |     |          |    |           |    |
| 2d (13-14 Oct)            | 914     | 169    |     | 127       |     | 10,2     |    | 11,6      |    |
| 3d (14-15 Oct)            | 1270    | 145    |     | 51        |     | 11,4     |    | 6,5       |    |
| 4th (15-16 Oct)           | 1225    | 291    | 202 | 84        | 118 | 13,8     | 37 | 8,4       | 35 |
| 5th (16-17 Oct)           | 1080    | 188    | 202 | 55        | 82  | 11,8     | 37 | 8,1       | 31 |
| 6th (17-18 Oct)           | 2400    | 248    |     | 87        |     | 14,4     |    | 13,9      |    |
| 7th (18-19 Oct)           | 1045    | 122    |     | 68        |     | 10,8     |    | 10,0      |    |
| 12th (24-25 Oct)          | 1170    | 107    |     | 39        |     | 5,1      |    | 3,9       |    |
| FLE                       |         |        |     |           |     |          |    |           |    |
| Before spaceflight (n=20) | 1041±94 | 182±22 | 225 | 81±12     | 88  | 12,8±1,8 | 62 | 7,5±0,9   | 37 |
| After:                    |         |        |     |           |     |          |    |           |    |
| 2d (13-14 Oct)            | 1410    | 315    |     | 118       |     | 27,2     |    | 7,1       |    |
| 3d (14-15 Oct)            | 1090    | 238    |     | 66        |     | 17,6     |    | 9,0       |    |
| 4th (15-16 Oct)           | 830     | 186    | 202 | 51        | 118 | 13,6     | 37 | 7,0       | 35 |
| 5th (16-17 Oct)           | 840     | 207    | 202 | 49        | 82  | 18,0     | 37 | 9,0       | 31 |
| 6th (17-18 Oct)           | 1100    | 191    |     | 53        |     | 9,0      |    | 5,0       |    |
| 7th (18-19 Oct)           | 1045    | 168    |     | 61        |     | 16,7     |    | 9,5       |    |
| 12th (24-25 Oct)          | 1140    | 129    |     | 29        |     | 12,6     |    | 7,2       |    |

After the spaceflight there was no change in plasma renin activity in the FLE, while blood aldosterone concentration on L+1 was 1/15th the background value and on the 7th postflight day was only 58% of that level. This is what apparently caused the corresponding excretion of ions by the kidneys.

The findings are indicative of basically different changes in sodium excretion and activity of the renin-angiotensin-aldosterone system postflight in the CDR and FLE. One of the causes of the differences found in the FLE could have been retention of increased delivery of blood to thoracic organ vessels, which is inherent in weightlessness. This was probably indicative of delayed readaptation of regional hemodynamics to earth's gravity after the long-term spaceflight. Its recovery apparently began on the 7th-12th day, when FLE showed retention of sodium (see Table 2).

Unlike the findings referable to flights of shorter duration, on the 1st day after the spaceflight both cosmonauts presented a lower total calcium and its ionized fraction level in blood serum than before the flight and it was somewhat lower than the mean statistical data for a healthy man (Table 3). In the CDR, PTH content of blood was considerably below mean values, while CT level was virtually at the mean statistical level (see Table 3). In the FLE, the decrease in PTH concentration, though it was less marked, was associated with decline of blood CT level. In both cosmonauts (but more so in FLE), calcium excretion in urine was greater, as was

the case after earlier long-term spaceflights, than before the mission. Considering that calcium intake with food was lower in the postflight period than before the mission (see Table 2), it can be considered that a negative

Table 3.

| Day of examination | Calcium |         | PTH  | CT  |
|--------------------|---------|---------|------|-----|
|                    | total   | ionized |      |     |
| CDR                |         |         |      |     |
| Before flight      | 4,61    | 1,09    | 0,20 | 214 |
| After:             |         |         |      |     |
| 1st                | 4,05    | 0,98    | 0,10 | 196 |
| 7th                | 4,48    | 1,06    | 0,20 | 286 |
| FLE                |         |         |      |     |
| Before flight      | 4,73    | 1,12    | 0,20 | 214 |
| After:             |         |         |      |     |
| 1st                | 4,21    | 1,00    | 0,17 | 147 |
| 7th                | 4,61    | 1,04    | 0,21 | 335 |

calcium balance persisted in both cosmonauts in the recovery period. The increased elimination of this ion by the kidneys with low level of its ionized fraction in blood and little change in glomerular filtration could be related to decreased reabsorption of calcium ions in the renal tubules. This could have been caused by the effect of CT on renal tubule cells against the background of relative decline in blood PTH. The dynamics of restoration of blood calcium and PTH in the postflight period could serve as confirmation of this (see Table 3). On L+7, levels of PTH and ionized calcium were within the range of the physiological norm, although  $Ca^{2+}$  did not reach the preflight level. At the same time, CT content increased and was above

the mean for a healthy man. Elimination of calcium by the kidneys was greater than in the background period.

For the first time, hypocalcemia was demonstrated after a long-term spaceflight. From the standpoint of predicting possible consequences of impairment of calcium metabolism when exposed to weightlessness for a long time, we are alerted by the fact that a negative balance of this ion in blood is observed with decline of ionized calcium level.

A load test with potassium chloride was performed before the spaceflight and on L+2 in order to examine renal function. As a result, it was established that, at the time of the postflight test, urine potassium concentration showed almost a 2-fold increase in both cosmonauts. Elimination of fluid decreased to one-half. As a result, there was a tendency toward faster excretion of potassium and its elimination within 4 h of the test. After the preceding 175-day spaceflight, there was more marked excretion of this ion. Changes in sodium elimination were different in CDR and FLE; in the former, there was decreased excretion of the ion in urine, whereas in the latter excretion exceeded background values during the test (Figures 1 and 2).

During the load test, both cosmonauts presented faster excretion of calcium and magnesium during the period of maximum kaliuresis, as compared to the preflight test. Total excretion of bivalent ions in the 4-h test (see Figures 1 and 2) was also greater than in the preflight period. Such changes were observed also when the test was made after the 175-day spaceflight, as well as in a test with 2% water load following a 96-day spaceflight and, in some cases, after short-term flights [5].

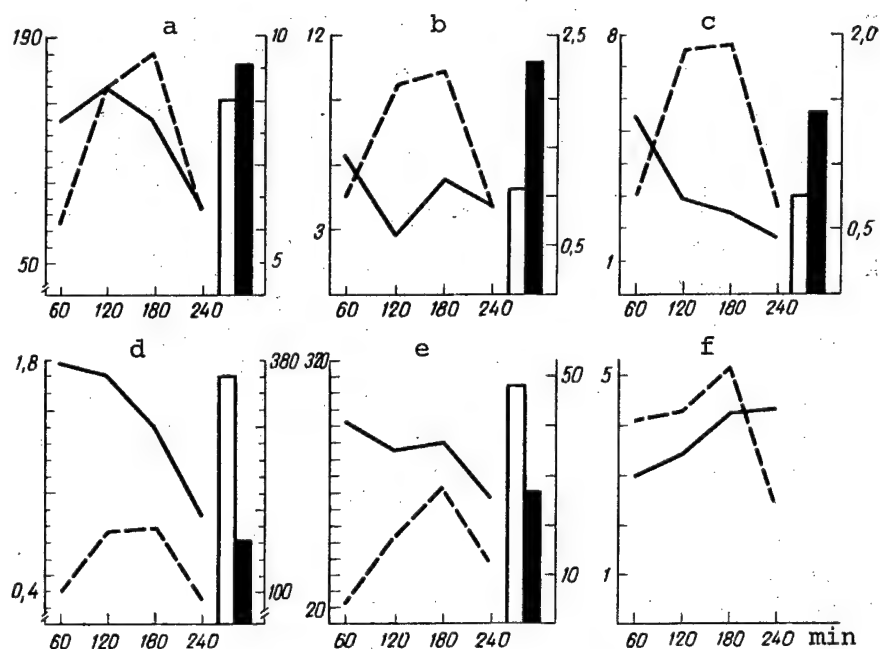


Figure 1. Dynamics of diuresis, rate of excretion of electrolytes, in  $\mu\text{eq}/\text{min}$ , and aldosterone, in  $\text{pg}/\text{min}$ , during potassium test on CDR before (solid line) and after (dash line) spaceflight.  
Here and in Figure 2: Bars represent excretion in  $\text{meq}$  during 4-h test before (white bars) and after (black bars) spaceflight  
a) potassium b) calcium c) magnesium d) fluid e) sodium f) aldosterone

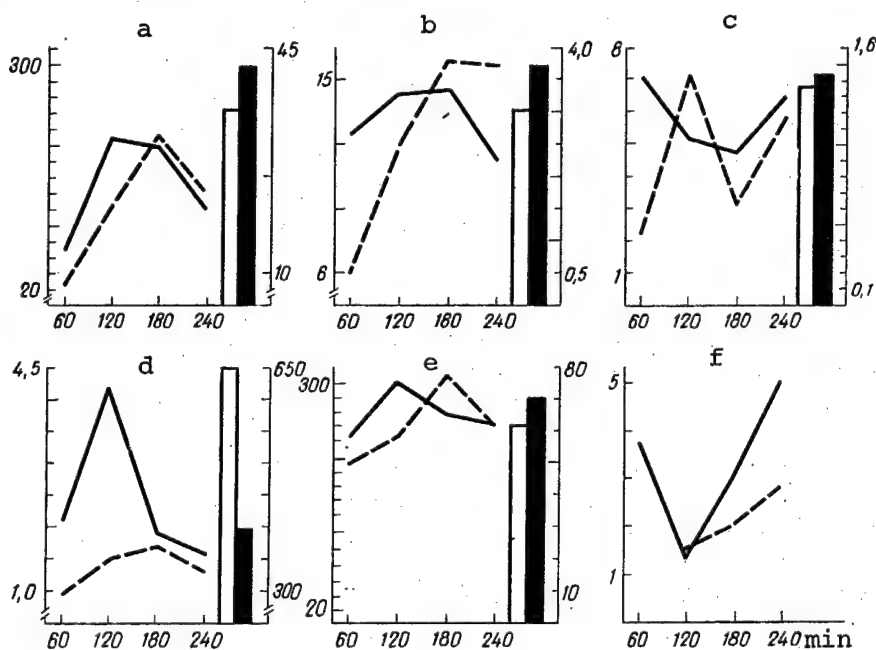


Figure 2. Dynamics of diuresis, rate of excretion of electrolytes and aldosterone during potassium test in FLE before (solid line) and after (dash line) spaceflight

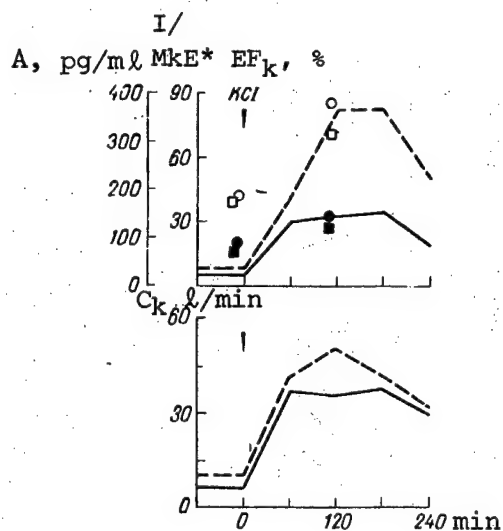


Figure 3.

Dynamics of elimination of potassium and its excreted fraction (EF), insulin (I) and aldosterone (A) content in blood during potassium test before and on 158th day of bedrest. Black circles and squares--aldosterone and insuline levels in background period. Solid line--EF in background period, dash line--during bedrest

\*MkE--expansion unknown

who have participated in missions of varying duration, there was marked retention of fluid and sodium. Conversely, in the FLE sodium excretion in urine exceeded preflight values. These differences were attributable to individual distinctions of regional hemodynamics, as a result of which there were changes in different directions in activity of the renin-angiotensin-aldosterone system.

Along with changes in excretion of monovalent ions in urine, there was increased elimination of bivalent ions. The increase in calcium excretion in urine occurred against a background of diminished concentration of total and ionized calcium, PTH and CT.

During the load test with potassium chloride, we observed increased potassium excretion during the 4-h test and in the period of maximum diuresis, which we interpreted as inability of body tissues to retain potassium after the spaceflight due to atrophic processes that developed in the muscles under the effect of weightlessness.

Apparently the increased excretion of potassium against the background of a decrease in its concentration in blood and of calcium with a low level in serum were caused by the tissues' inability to retain ions as a result of atrophic processes, which develop in weightlessness due to lack of load on the skeleto-muscular system. Changes in hormonal status were also rather significant. Thus, excretion of aldosterone in urine during the test was higher in the CDR after the spaceflight than preflight, whereas in the FLE it was lower (see Figures 1 and 2). We had previously demonstrated substantial changes in hormonal activity during exposure of people to simulated weightlessness during 182-day hypokinesia with head-down tilt (Figure 3). Analogous changes in blood hormone levels could apparently also occur after the 185-day spaceflight, and this perhaps caused the distinctions in ion elimination during the load test in the postflight period.

Thus, after the 185-day spaceflight, we demonstrated different changes in fluid-electrolyte metabolism and systems of its regulation in the CDR and FLE. In the CDR, as in most cosmonauts

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TOLERANCE TO +Gz AND +Gx ACCELERATIONS OF INDIVIDUALS IN OLDER AGE GROUPS  
IN GOOD HEALTH AND WITH EARLY SIGNS OF ATHEROSCLEROSIS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19,  
No 3, May-Jun 85 (manuscript received 20 Mar 84) pp 27-31

[Article by A. R. Kotovskaya, D. G. Dimitrov, V. Yu. Luk'yanyuk, I. F. Vil'-Vil'yams, O. L. Golovkina, V. G. Andreyeva, N. P. Artamonova and M. P. Kuz'min (People's Republic of Bulgaria and USSR)]

[English abstract from source] Tolerance to +Gz and +Gx accelerations of healthy and atherosclerotic subjects, aged 40-49, was investigated during 256 centrifugation tests in Bulgaria and the USSR. As compared to the healthy people, the atherosclerotic subjects showed a lower tolerance: when exposed to 7+Gz the tolerance threshold decreased from  $5.93 \pm 0.57$  g to  $5.7 \pm 0.44$  g (i.e. by 0.23 g). Visual disorders in the healthy and atherosclerotic subjects were recorded in 29 and 50%, respectively, and loss of consciousness in 9.56 and 15.15%, respectively (Bulgarian data). When exposed to 5 +Gz and 6 +Gx no subjects displayed visual disorders or loss of consciousness (Soviet data). However, lower tolerance of 5 +Gz due to cardiac arrhythmias was observed in 4.8% atherosclerotic patients and in none healthy subjects. Lower tolerance to 6 +Gx associated with cardiac arrhythmias was recorded in 23.8% atherosclerotic versus 11.8% healthy subjects (i.e. 12% more). Nevertheless, in most subjects, both healthy and atherosclerotic, acceleration tolerance was good. These findings indicate that individual assessment of acceleration tolerance is of great importance for people older than 40 years with health abnormalities.

[Text] Development of cosmonautics opens up the prospects of having highly qualified specialists of different ages participate in future space missions, including individuals over 40 years of age with deviations in health status.

There are many works in the literature dealing with tolerance to accelerations that describe investigations of tolerance to accelerations of individuals in older age groups. Some authors report a decline in tolerance to +Gz accelerations in subjects over 40 years of age [3], while others adhere to a

different opinion. According to P. V. Vasil'yev and A. R. Kotovskaya [1], there are no distinct changes in tolerance to transverse +Gx accelerations with advance in age.

After simulating the effects of weightlessness with hypokinesia lasting 10.5 days, American authors observed a decrease in tolerance to +Gz accelerations in subjects over 40 years old [6].

It is also known that older individuals with health abnormalities in the form of neurocirculatory dystonia of the hypertensive and cardiac types, essential hypertension grade I tolerance to +Gz accelerations is poorer than in healthy subjects [4].

The most frequent deviation in health status associated with aging is development of atherosclerosis [2]. However, there have been no studies of tolerance to accelerations of subjects with early signs of atherosclerosis (ESA).

Our objective here was to investigate tolerance to various modes of +Gz and +Gx accelerations by subjects over 40 years old with ESA and essentially healthy subjects of the same age.

#### Methods

A total of 256 tests of tolerance to accelerations by subjects in older age groups were performed on centrifuges in Bulgaria and the USSR. A total of 191 people were tested. Of this number, 57 had ESA and 134 were essentially healthy (control).

All of the studies were divided into three series.

In the first series, tests were performed in Bulgaria on 177 subjects. Of this number, 127 subjects 35-39 years old were in good health and 50 40-45 years old suffered from ESA without clinical manifestations. The diagnosis of ESA in these cases was made on the basis of changes in the rheoencephalogram (REG). The subjects were submitted to head-pelvis (+Gz) accelerations of 4, 5, 6 and 6.5-7.0 G for 30 s at a time up to tolerance limit with build-up gradient of 1.3-1.5 G/s.

In the second and third series, which were performed in the USSR, there were tests on 14 subjects 40 to 49 years old. Seven of them were essentially healthy and seven had ESA. The diagnosis of ESA was made on the basis of changes in the REG and the following clinical manifestations of disease: accent on second sound on the aorta, systolic murmur upon auscultation of the heart, roentgenological signs of atherosclerosis of the aorta, changes in vessels of the optic fundus and lipid metabolism disorders. In the second series of studies, the subjects were submitted to head-pelvis (+Gz) accelerations of 3, 4 and 5 G, for 30 s each and in the third series, to chest-back (+Gx) accelerations of 4 and 6 G, for 60 s each. The build-up gradient was 0.2 G/s.

In the first and second series, the back of the chair was tilted at an angle of 12° in relation to the vector of acceleration and in the third, 78°. In all series, the subjects remained seated with 70-80° flexion in the hip and knee joints.

In all of the tests, we recorded heart rate (HR), ECG in the Nehb leads, arterial pressure (BP) in the brachial artery according to Korotkov sounds, systolic BP in vessels of the earlobe, which reflects circulation in cerebral vessels.

The tests were conducted without use of anti-G gear. In order to enhance tolerance to accelerations, all of the subjects produced static muscular tension of the prelum abdominale and lower extremities during speed build-up of the centrifuge and at plateaus.

All of the data were processed by the Student method of variation statistics.

## Results and Discussion

According to the data of the Bulgarian studies, in the first series the limit of tolerance to +Gz accelerations constituted a mean of  $5.93 \pm 0.57$  G in healthy subjects. It was 0.23 G lower in those with ESA and constituted a mean of  $5.7 \pm 0.44$  G (Figure 1).

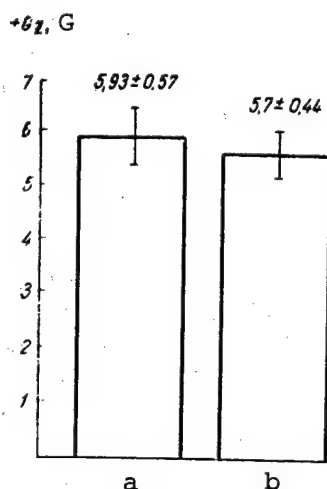


Figure 1.

Range of tolerance to +Gz accelerations on Bulgarian centrifuge in healthy subjects 35-39 years old (a) and subjects with ESA 40-45 years old (b)

White regions, good and satisfactory tolerance; crosshatched, diminished tolerance\*

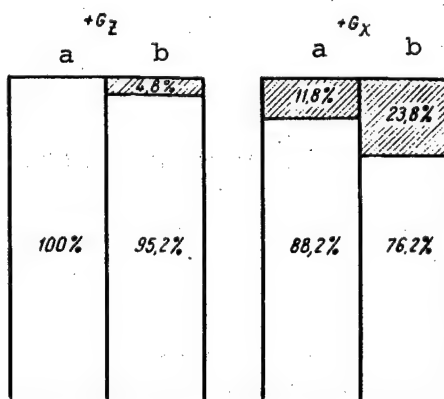


Figure 2.

Tolerance to +Gz accelerations of up to 5 G and +Gx up to 6 G on USSR centrifuge in healthy subjects (a) and individuals with ESA (b) 40-49 years of age

Visual disorders were the main symptom that limited tolerance to accelerations of healthy subjects and those with ESA. At the same time, some of the subjects tolerated accelerations without visual disorders. In healthy subjects,

\*Translator's note: no markings are present in bars of figure in source.

functional visual disorders were demonstrated in 29% of the cases and in those with ESA, in 50%. These data indicate that there were 21% more visual disorders among subjects with ESA than healthy ones.

After appearance of visual disorders in the form of a black veil in some subjects we observed loss of consciousness, which was probably related to hemodynamic disturbances due to the relatively rapid build-up of accelerations (1.3-1.5 G/s). Loss of consciousness was observed in 9.56% of the healthy subjects and 15.15% of those with ESA (i.e., 5.59% more often than in healthy subjects).

With exposure to maximum +Gz accelerations, heart rate rose on the average from  $82 \pm 14$  to  $147 \pm 12$ /min in healthy subjects and from  $80 \pm 13$  to  $149 \pm 11$ /min in those with ESA. We failed to observe significant differences between healthy subjects and those with ESA with respect to dynamics of HR.

In both groups we demonstrated heart rhythm disturbances in the form of extrasystolic arrhythmia in 17.4% of the cases. There were no appreciable differences in incidence and nature of rhythm disorders between parameters of subjects in the two groups.

Systolic BP in earlobe vessels dropped in all subjects on the average from 108-124 to 80-100 mm Hg. When visual disorders developed in the form of a black veil, earlobe vessel BP was below 40 mm Hg. We did not observe statistically significant differences between healthy subjects and those with ESA with regard to changes in this parameter.

Systolic BP in the brachial artery rose in all subjects on the average from 120-129 to 159-175 mm Hg and diastolic, from 76-88 to 88-100 mm Hg. There were no appreciable differences between the subjects in dynamics of systolic and diastolic BP.

In the second series of tests conducted in the USSR, in which milder accelerations were used than in Bulgaria, all of the subjects tolerated well +Gz accelerations up to 5 G. There were no visual disturbances or loss of consciousness.

HR increased on the average from  $75 \pm 7$  to  $147 \pm 9$ /min in healthy subjects and from  $83 \pm 4$  to  $141 \pm 6$ /min in those with ESA. There were no statistically significant differences between parameters of these groups of subjects with regard to HR changes.

Extrasystolic arrhythmia was the main form of cardiac rhythm disturbances in all subjects (see Table). Subjects with ESA had 9 times more extrasystoles than healthy ones. Serious forms of extrasystolic arrhythmia, in the form of group, polytopic and multiple extrasystoles were observed only in subjects with ESA (4.8% of the cases). These findings are indicative of diminished tolerance to +Gz of 5 G in 4.8% of the subjects with ESA. In the other 85.2% of subjects with ESA and 100% of the healthy subjects tolerance to accelerations was good (Figure 2).

Systolic BP of earlobe vessels changed on the average from 116-129 to 125-131 mm Hg in healthy subjects and those with ESA. Systolic BP in the brachial artery rose from 119-120 to 209-214 mm Hg and diastolic, from 79-85 to

130-157 mm Hg. There were no statistically significant differences between healthy subjects and those with ESA in changes in these parameters.

Incidence and nature of arrhythmias under effect of +Gz accelerations up to 5 G and +Gx to 6 G in healthy and ESA subjects 40-49 years of age

| Accelerations | Subjects | Number of subjects | Subjects with dysrhythm. | Number of extrasystoles |          |                             |                  |             | Number of sinoatrial blocks |
|---------------|----------|--------------------|--------------------------|-------------------------|----------|-----------------------------|------------------|-------------|-----------------------------|
|               |          |                    |                          | total                   | isolated | multiple*, group & bigeminy | supraventricular | ventricular |                             |
| +Gz           | Healthy  | 20                 | 2                        | 2                       | 2        | 0                           | 2                | 0           | 0                           |
|               | With ESA | 21                 | 6                        | 18                      | 6        | 12                          | 8                | 10          | 1                           |
| +Gx           | Healthy  | 17                 | 8                        | 23                      | 14       | 9                           | 21               | 2           | 0                           |
|               | With ESA | 21                 | 10                       | 67                      | 27       | 40                          | 47               | 20          | 0                           |

\*Five or more extrasystoles.

In the 3d series of studies, also conducted in the USSR, all subjects tolerated +Gx accelerations to 6G without visual disorders or loss of consciousness.

HR rose on the average from  $68 \pm 6$  to  $110 \pm 14$ /min in healthy subjects and from  $74 \pm 3$  to  $96 \pm 7$ /min in those with ESA.

Heart rhythm disturbances in the form of extrasystolic arrhythmia were observed in healthy subjects and those with ESA. The latter had about 3 times more extrasystoles than healthy subjects (see Table). Serious forms of dysrhythmia in the form of group, polytopic and multiple extrasystoles were observed in 11.8% of the tests on healthy subjects and 23.8% of those with ESA (i.e., 12% more often than in healthy subjects). These findings are indicative of diminished tolerance to +Gx accelerations up to 6 G in these subjects. In the other 88.2% of the healthy subjects and 72.2% of those with ESA, tolerance to accelerations was good.

Systolic BP in brachial vessels rose on the average from 122-132 to 200-230 mm Hg and diastolic, from 75-80 to 123-134 mm Hg. There were no reliable differences between the healthy subjects and those with ESA demonstrable upon analysis of changes in these parameters.

Analysis of the experimental data revealed that tolerance to accelerations was either quite high (Bulgarian data) or good (USSR data) in most subjects over 40 years of age (healthy and with ESA).

At the same time, tolerance was low in some subjects (healthy and with ESA). Tolerance to accelerations was lower in subjects with ESA than in healthy ones.

The results of these investigations also revealed that the distinctions of physiological reactions to accelerations in subjects with ESA, as compared to healthy subjects, were a function of magnitude of accelerations.

Thus, at high values of +Gz accelerations (up to 7 G), individuals with ESA presented visual disorders and loss of consciousness more often than healthy

subjects. These changes were probably related to diminished compensatory capabilities of the cardiovascular system of older subjects with ESA under conditions of marked gravitational redistribution of blood.

At the same time, at lower +Gz accelerations (up to 5 G) and with +Gx accelerations up to 6 G all of the subjects (healthy and with ESA) tolerated them without visual disorders or loss of consciousness.

The physiological reactions of subjects with ESA under the effect of accelerations also depended on the severity of atherosclerosis. Thus, in cases where there were no clinical signs of atherosclerosis and the diagnosis of this disease had been made only on the basis of REG changes, with +Gz accelerations dysrhythmia was observed in 17%. When signs of atherosclerosis of the aorta and other vessels were noted, impairment of cardiac rhythm was demonstrated in 28% of the cases (6 tests out of 21; see Table).

There are two groups of factors that probably play a part in the genesis of ectopic cardiac arrhythmia in older subjects exposed to accelerations. One group is related to impaired regulation of heart rhythm under gravitational stress. It includes functional changes in autonomic centers of regulation of the cardiovascular system, reflex influences that arise as a result of systemic and regional circulatory disturbances and shifting of organs, signs of myocardial hypoxia and decline of its energy resources [3-5].

The other group of factors is related to age-related distinctions of heart rhythm regulation. It is known that there is weakening of nervous influences on the heart with age, as well as decreased automatism of the sinus node; there is poorer conduction in some parts of the myocardium and sites of impaired metabolism are formed. The decrease in cellular potassium ions and increased sensitivity of the heart to catecholamines are also of some significance to development of cardiac arrhythmias in subjects over 40 years old. Myocardial hypoxia related to emptying of the capillary bed and atherosclerotic changes in the walls of coronary vessels also plays an important role in development of ectopic sites of excitation in older individuals during functional loads [2].

These findings are indicative of the special importance of individual expert evaluation of tolerance to accelerations of individuals over 40 years of age (both healthy and those with health deviations in the form of ESA).

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EFFECT OF HYPOKINESIA AND +Gz ACCELERATIONS ON TRANSPORT FUNCTION OF HUMAN BLOOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 13 May 83) pp 31-33

[Article by N. V. Khapilov, V. S. Panchenko, N. N. Kotov and B. F. Asyamolov]

[English abstract from source] The results of 44 studies of circulation parameters and blood transport function of 14 test subjects exposed to 7-day bed rest ( $-10^\circ$  head-down tilt) and acceleration of 4.5 Gz have demonstrated that the blood transport carriers and their actively binding centers form working structures in the adaptive reactions. As compared to the pre-test level, the distribution ratio of  $^{14}\text{C}$ -adenine between two immiscible phases (plasma/oil, erythrocytes/oil) varies from -12 to 14% on bed rest day 3 to +32 to 40% on bed rest day 7; it increases by 145-150% after exposure to +4.5 Gz acceleration. The parameters of the blood transport function give a quantitative description of its adaptive reactions to environmental effects.

[Text] Biopolymers differing in structure and function (proteins, lipoproteins, enzymes, nucleic acids, etc.) contained in blood plasma, lymph and interstitial fluid are elements of the body's transport system [10]. The results of studies pursued in recent years revealed that there is a close relationship between the transport system and functional changes in the body [1, 6, 8, 10].

Hypodynamia is one of the factors that have an adverse effect on the body during long-term spaceflights. As we know, it causes increase in blood and liver cholesterol content, adaptive changes in protein composition of blood, alters free-radical processes and is instrumental in a number of other functional changes [2-5, 7, 9].

Data obtained in studies of metabolic processes with use of the results of spaceflights and transport systems confirmed the results of model experiments with regard to alteration of the protein spectrum of blood [3, 5, 9]. However, some questions are still unclear, which deal with the effects of hypodynamia, accelerations and other adverse flight factors directly on blood transport function.

Our objective here was to assess changes in transport functions of blood as one of the indicators of functional state of the body during simulation of negative spaceflight factors with hypokinesia and accelerations.

In addition, it was important to establish the existence of a relationship between hemodynamic parameters generally used in such cases to monitor the functional state and transport characteristics of blood.

## Methods

There was a total of 44 studies with the participation of 14 men 20 to 30 years old who spent 7 days under antiorthostatic hypokinetic conditions at an angle of  $-10^\circ$ . Before and after hypokinesia, the subjects were submitted to +Gz accelerations of up to 4.5 G. Blood was drawn in amounts of no more than 5 ml per test to examine the effect of hypokinesia and accelerations on transport function. Blood was drawn before hypokinesia, on the 3d and 7th days of hypokinesia and after generating accelerations on the centrifuge.

Determination of transport parameters of blood fractions was made by the method of immiscible phases according to coefficients of distribution of labeled ligand.

We used the following immiscible phases: blood plasma-oil, red blood cell suspension-oil.

We used  $^{14}\text{C}$ -adenine as labeled ligand. Blood was first incubated with the ligand for 10-15 min. After incubation we formed systems of immiscible phases: blood fractions-cedar or olive oil in volumes of no more than 1.5 ml per phase. The systems of phases were mixed, and we measured by the radio-metric method the level of labeled adenine in each phase. The ratio between amount of radioactive tracer in each phase was taken as the coefficient of distribution. We assessed the degree of binding of low-molecular nonelectrolyte by high-molecular protein transport carriers of blood according to the coefficient of distribution of radioactive adenine in phases.

The mechanism of redistribution of low-molecular nonelectrolyte in two immiscible phases is simple. The amount of tracer in the oil phase depends on the state of blood protein fractions and change in their binding capacity under the influence of physicochemical factors.

Concurrently, we recorded the ECG in the second standard lead and body rheogram according to Kubicek.

We took into consideration the subjects' general condition and appearance. Pulse rate (PR), cardiac output (CO), circulation volume (CV) and duration of expulsion of blood from the left ventricle (E) were determined using averaged data (for 5-min intervals). Hemodynamic parameters were recorded before hypokinesia in horizontal position and on the 3d and 7th days of the study in antiorthostatic position. The data were processed by the method of variation statistics.

## Results and Discussion

The subjects' condition was satisfactory at all times.

On the 3d day of hypokinesia, the coefficient of distribution of  $^{14}\text{C}$ -adenine in phases dropped 12-14% from the base level. In this time, there were changes in hemodynamic parameters within the range of usual deviations inherent in the tested conditions.

On the 7th day of hypokinesia, the coefficient of distribution of  $^{14}\text{C}$ -adenine in plasma-oil ( $K_{po}$ ) and erythrocytes-oil ( $K_{eo}$ ) phases increased by 32-40% in relation to the base level. Hemodynamic parameters changed accordingly within a certain range (see Table).

Change in hemodynamic parameters and coefficient of distribution of  $^{14}\text{C}$ -adenine in plasma-erythrocytes-oil system during 7-day hypokinesia ( $M \pm m$ )

| Time of test        | PR/min         | CO, ml          | CV, ml         | $E_m$             | $K_{po}$        | $K_{eo}$        |
|---------------------|----------------|-----------------|----------------|-------------------|-----------------|-----------------|
| Control             | $61.7 \pm 2.2$ | $93.7 \pm 3.2$  | $5781 \pm 292$ | $0.306 \pm 0.003$ | $2.04 \pm 0.15$ | $3.14 \pm 0.25$ |
| Day of hypokinesia: |                |                 |                |                   |                 |                 |
| 3                   | $54.7 \pm 2.0$ | $103.8 \pm 5.7$ | $5678 \pm 311$ | $0.269 \pm 0.01$  | $1.79 \pm 0.27$ | $2.7 \pm 0.15$  |
| 7                   | $58.5 \pm 2.5$ | $97 \pm 5.0$    | $5721 \pm 304$ | $0.288 \pm 0.01$  | $2.7 \pm 0.23$  | $4.42 \pm 0.35$ |

The demonstrated changes in hemodynamic parameters and blood transport function indicate that adaptive alteration of the body under hypokinetic conditions is referable not only to hemodynamics, but active centers of transport carriers.

This adaptive fluctuations in functional activity of organs according to transport parameters of blood, in particular for each period of hypokinesia, have their own significance.

After generation of accelerations of up to 4.5 G, the coefficient of distribution of  $^{14}\text{C}$ -adenine in plasma and erythrocytes in relation to oil increased by 145-150% (coefficient of distribution of  $^{14}\text{C}$ -adenine in the plasma-oil system acquired a value of  $5 \pm 0.86$  and in the erythrocytes-oil system,  $7.9 \pm 0.7$ ).

Thus, hypokinesia and accelerations alter appreciably the binding capacity of blood transport carriers, which is indicative of their active participation in forming the adaptive reactions of the body to these factors. It should also be noted that strictly specific parameters of transport function of blood and hemodynamics correspond to a specific functional state of the body.

Analysis of the findings warrants the conclusion that it is necessary to take into consideration parameters of transport function of blood as one of the important criteria reflecting quantitative adaptive fluctuations of its

functional activity in response to exogenous environmental factors in order to comprehend the mechanism of functional changes under the effect of hypokinesia and accelerations, along with the conventional parameters.

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OXYGENATION AND REGIONAL CIRCULATION IN GINGIVAL MUCOSA DURING EXPOSURE  
TO LOWER BODY NEGATIVE PRESSURE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19,  
No 3, May-Jun 85 (manuscript received 18 Jul 83) pp 33-37

[Article by S. I. Vol'vach, Ye. A. Kovalenko, S. I. Ponomarev, V. K. Gabyshev,  
V. I. Nikiforov, A. P. Kulev and V. V. Arkhipov]

[English abstract from source] Five test subjects were exposed to lower body negative pressure (LBNP). During exposure their regional circulation and oxygen balance of the gingival mucosa were measured and electrocardiography and kinetocardiography were performed to calculate parameters of the left heart function. The study showed a distinct correlation between LBNP tolerance and the level of compensatory reactions of the gingival mucosa blood flow and the cardiovascular system as a whole. The subjects with a high LBNP tolerance showed well pronounced regional compensatory reactions of the gingival mucosa that were not accompanied by significant changes in the left heart function. The subjects with a moderate tolerance exhibited either weak or no regional compensatory reactions of the gingival mucosa and significant changes in the left heart function.

[Text] Exposure to lower body negative pressure (LBNP) elicits changes in central hemodynamics.

The dynamics of parameters of regional blood flow and, particularly, delivery of oxygen to tissues in the basin of blood supply to the carotid artery could serve as an objective criterion to assess degree of possible hypoxia and effectiveness of compensatory reactions. Our objective here was to use a combined rheopolarographic method to examine oxygenation and circulation in the gingival mucosa in order to assess the effectiveness of compensatory reactions of the cardiovascular system to LBNP.

#### Methods

The study was conducted on 5 essentially healthy men 25-35 years of age at relative rest and during LBNP in the following modes: -25 mm Hg for 2 min,

-35 mm Hg for 3 min, -40 mm Hg for 5 min and -50 mm Hg for 5 min; recovery period constituted 10 min. We conducted 18 tests in all. The electrocardiogram (ECG) and kinetocardiogram (KCG) of the left heart were recorded on each subject both at rest and during LBNP. In order to assess the functional state of the system of regional circulation and oxygenation of tissues of the gingival mucosa, we recorded the rheogram (RG) and polarogram (PG) of the tested region of the gingival mucosa [4]. The KCG was interpreted by the method of L. B. Andreyeva and N. B. Andreyeva [1], as modified by V. A. Degtyarev. We measured the intervals of the cardiac cycle (R-R), periods of asynchronous contraction (AC), isometric contraction (IC), rapid ejection ( $E_m$ ), slow ejection ( $E_r$ ), protodiastole (P), isometric relaxation, rapid filling ( $F_r$ ), slow filling ( $D_y$ ) and atrial systole. The area of the aortic lumen was determined from the nomogram published in [6], then the formula in [5] was used to calculate on a computer the following parameters: stroke volume (SV), phasic volume of the heart during rapid ejection of blood from ventricle (amount of blood ejected from left ventricle during rapid ejection period;  $PV_1$ ); phasic heart volume during slow ejection of blood ( $PV_2$ ); phasic heart volume during rapid filling of left ventricle ( $PV_3$ ); phasic volume during slow filling of left ventricle ( $PV_4$ ) and phasic heart volume during left atrial systole ( $PV_5$ ).

In interpreting the RG we determined the rheographic index (RI). The method of Ye. A. Kovalenko et al. [2] was used to interpret the PG and calculate  $pO_2$  in tissues of the gingival mucosa.

Since we examined oxygenation and regional circulation in the gingival mucosa, special attention was given to the clinical status of the periodontium of all subjects. Periodontial tissue showed no visible pathological changes in two subjects, insignificant gingivitis was found in one and early stage of periodontosis in two subjects. These changes in the periodontium did not elicit any marked base changes in the tested rheogram and polarogram parameters.

## Results and Discussion

At the first stage of LBNP all subjects presented a marked decline of  $pO_2$  and RI in tissues of the gingival mucosa. However, the severity of these disturbances and degree of compensatory reactions were not the same.

In subjects with good tolerance to LBNP, we observed already in the 2d min of exposure a distinct compensatory reaction in the gingival mucosal circulation, which was characterized by elevation of RI and  $pO_2$ . The dynamics of  $pO_2$  presented distinct periodicity of fluctuations: with increase in LBNP this parameter declined in the examined tissues, but after 1-2 min (after the body's adaptation to the new state) there was a rise (Figure 1). In subjects with good tolerance to LBNP and a well-pronounced compensatory reaction of the gingival mucosal circulation, pulse rate increased by a mean of 25%, while cardiac output increased by 13.6%. SV held at close to the base level due to insignificant changes in volume and period parameters of the left heart (Figure 2).

In subjects with satisfactory tolerance to LBNP, there were either no compensatory reactions on the part of vessels of the gingival mucosa, or else they were insignificant in magnitude and duration. There was also no periodicity to

dynamics of  $pO_2$ , and 2 subjects developed a presyncopic state in the 5th min of -50 mm Hg LBNP, which was associated with drastic drop of  $pO_2$  in tissues of the gingival mucosa. In subjects with poor compensatory reaction of the vascular system of the gingival mucosa, pulse rate increased by a mean of 55% and cardiac output, by 41%. SV held at close to the base level due to more marked changes in volume and phase characteristics of the left heart. These changes were the most marked in one of the subjects with strong reaction to LBNP, and they were associated with significant decline of  $pO_2$  and virtually no compensatory reactions by vessels of the gingival mucosa. In another subject with satisfactory tolerance to LBNP, the  $pO_2$  drop in tissues of the gingival mucosa was the most marked, and he also presented the lowest SV (even at rest), as well as significant changes in volumetric and phase parameters during LBNP (see Figures 1 and 2).

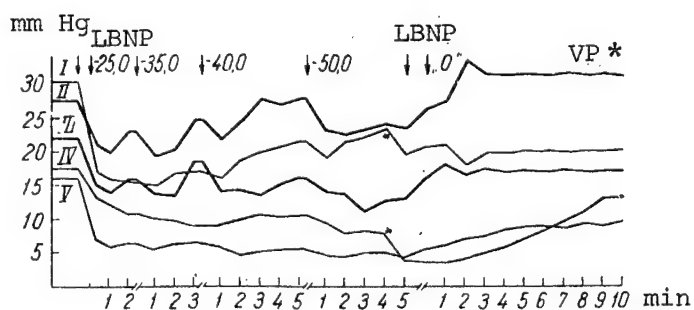


Figure 1.  
Dynamics of tissue  $pO_2$  of  
gingival mucosa during LBNP  
(mm Hg)

Vertical arrowheads show  
rarefaction in vacuum gear  
(mm Hg). The points on the  
curves show time of drastic  
worsening of wellbeing of  
subjects I and IV

\* VP--expansion unknown

We were impressed by the fact that with both good and poor tolerance to LBNP, the average decline of SV during LBNP was virtually the same: 9.5-9.8%. We could have also expected the same changes in both groups with respect to cardiac activity for compensation of tissular hypoxia. Our findings indicate the opposite. In subjects with a well-marked compensatory reaction of vessels of the gingival mucosa the changes in cardiac activity were less marked and, on the contrary, in subjects with satisfactory tolerance and minimal compensatory reactions of gingival mucosal vessels the changes in the cardiovascular system were more significant. Hence, the degree of compensatory reactions of the cardiovascular system is apparently inversely proportional to degree of compensatory reactions of local vessels in this region.

It is known that centralization of circulation, because of which systemic circulation is maintained in vital organs, is one of the mechanisms of maintaining viability of organs in extreme states. The number of functional capillaries in tissues and, consequently, delivery of oxygen to them under various extreme conditions depend largely as well on activity of arterio-venous anastomoses (AVA). It is known that expressly capillaries perform a greater oxygen-delivering function [3]. It can be assumed that the periodicity of  $pO_2$  dynamics observed in subjects with good tolerance to LBNP is attributable to general centralization of blood flow and redistribution of blood passing to these regions over a large number of nutritive capillaries due to closed AVA. In cases where circulatory hypoxia of head tissues,

including the gingival mucosa, is compensated by marked general redistribution of blood and redistribution of capillary blood flow on the microcirculatory level, there is no need for change in heart function and increase in cardiac output. The heart functions in a more economic mode and provides for adequate delivery of blood to tissues throughout the LBNP period by means of effective reactions of redistribution and retention of blood in the head region. This is confirmed by the less marked changes in cardiac activity expressly in subjects with good tolerance of LBNP, as observed in our investigation. In subjects with satisfactory tolerance to LBNP, because of inadequate compensatory reactions there is impaired regulation of AVA activity and compensatory redistribution of capillary blood flow is insufficient during exposure to extreme factors. When tissues cannot compensate for circulatory hypoxia, it becomes necessary to have greater influx of blood and, consequently, greater cardiac output. The heart functions in a stressed mode, there is considerable change in volume and phase parameters of left heart function. As a result, the limit of compensatory capacities of the cardiovascular system is reached rapidly, and there could be drastic deterioration of wellbeing (to the extent of unconsciousness).

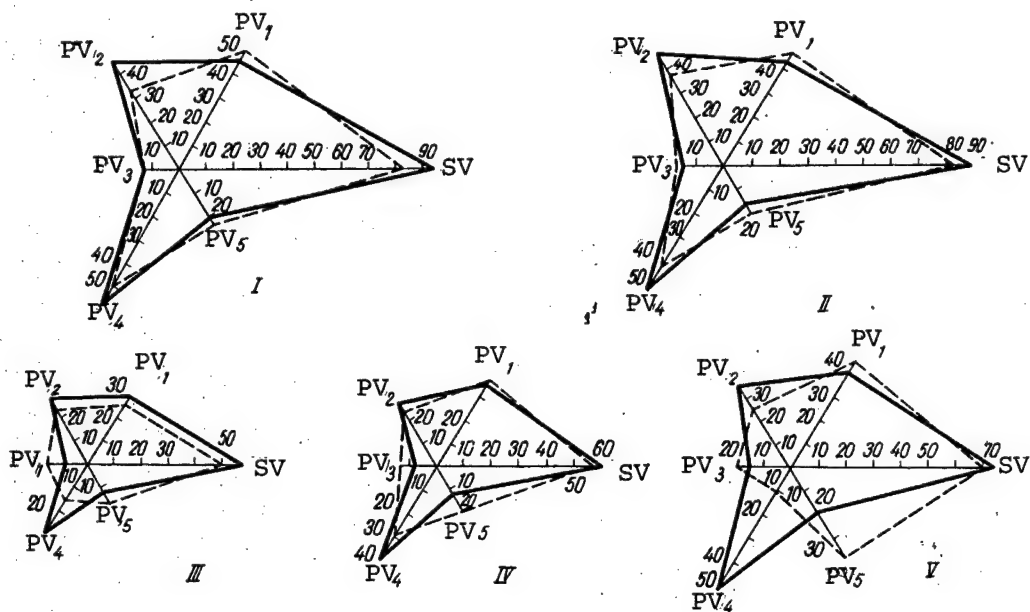


Figure 2. Polar diagrams of volume and phase function of the left heart at rest and with LBNP (mℓ)

Horizontal ray to the right of the center of the diagram shows SV values. The other rays show on the same scale the volume and phase parameters, upon which depends SV value. Boldface lines--at rest, dash lines--with exposure to LBNP (-50 mm Hg). I-V--subjects

On the basis of this investigation, it can be concluded that use of the combined rheopolarographic method enables us to assess blood supply to tissues of the gingival mucosa and its oxygenation under the effect of LBNP. In the presence of circulatory hypoxia, which develops with LBNP, reflex regulation

of vascular and cardiac activity are elements of compensatory reactions. The extent of systemic compensatory reactions on the part of the cardiovascular system is inversely proportional to the degree of regional compensatory reactions of vessels of the gingival mucosa.

Concurrent use of the combined method of studying oxygenation and regional circulation in the gingival mucosa, along with other methods of assessing heart function could be used as an objective test of human tolerance to LBNP.

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EFFECT OF WATER IMMERSION ON PARAMETERS OF CENTRAL HEMODYNAMICS IN INDIVIDUALS OVER 45 YEARS OLD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 3 Jan 83) pp 37-40

[Article by I. O. Fomin, V. N. Orlov, A. E. Radzevich and G. S. Leskin]

[English abstract from source] The effect of 7-day dry immersion on central hemodynamics of four test subjects, aged 46, with boundary arterial hypertension was investigated. The controls were two healthy men, aged 24. Central hemodynamics was examined by integrated rheography. Variations in blood pressure, central venous pressure, stroke and cardiac indexes, heart rate and total peripheral resistance were measured. The control subjects showed a decrease of blood pressure during exposure ( $P < 0.01$ ). Two of the test subjects with a short history of boundary arterial hypertension displayed similar variations ( $P < 0.01$ ), whereas two others showed an increase of blood pressure during the immersion period ( $P < 0.01$ ). The test and control subjects did not exhibit significant differences in the stroke and cardiac indexes, heart rate, central venous pressure or total peripheral resistance: stroke and cardiac indexes decreased while central venous pressure and total peripheral resistance increased, and heart rate remained unchanged.

[Text] Use of water immersion (WI) to reproduce the hemodynamic changes inherent in weightlessness proved its value in many studies [2, 10, 11, 12]. Until recently, the influence of immersion had been tested on healthy subjects 19 to 35 years of age. In these studies, duration of WI ranged from a few hours to 3-5 days [10, 12]. Development of the method of "dry" immersion made it possible to use long immersion procedures without danger of macerating the skin [8].

There are reports on the results of investigating some aspects of the effect of WI on individuals with borderline arterial hypertension (BAH) [4, 5, 9]. In subjects with this pathology, arterial pressure (BP) is in the range of 140/90-160/94 mm Hg, and diastolic pressure over 90 mm Hg is the most valuable diagnostic criterion for detection of BAH [3, 6].

In this investigation, we studied parameters of BP, stroke volume, cardiac output and central venous pressure in subjects over 45 years old with BAH during 7-day WI. For comparison purposes, we also tested healthy subjects.

## Methods

The dry-air immersion method [8] was used for WI. WI exposure lasted 7 days. We tested 6 men, 4 of whom had a history of BAH. These subjects made up the main group (MG). The average age of men in the main group was 46 years, height 172.5 cm, weight 84.25 and body area 1.98 m<sup>2</sup>; 2 subjects constituted the control group (CG). Their average age was 24 years, average height 174 cm, weight 71.5 kg and body area 1.86 m<sup>2</sup>.

To define the nature of BAH, we measured BP by the Korotkov method daily, every 2-3 h, starting 2 days before immersion, then during the entire WI period and for the first 2 recovery days. We calculated mean dynamic pressure ( $MBP = \frac{BPs + 2BPd}{3}$ ) and number of cases where BP exceeded 139/89 mm Hg. MBP was averaged for 2 days of the background period, entire WI period and we calculated its mean value separately for the 1st and 2d days of recovery ( $\overline{MBP} = \frac{\sum MBP}{n}$ ). To assess instability of cardiovascular system responses, we calculated the mean daily coefficient of covariation ( $CC + \frac{\sigma}{MBP} \cdot 100\%$ ).

The conditions were approximately identical during these 11 days for all subjects. We adhered to both a standard daily schedule and order of medical diagnostic procedures, which enabled us to detect distinctive BP reactions to various exogenous stimuli.

In addition to BP, we measured central venous pressure (CVP) by the method in [1] before WI, twice during WI (on 3d and 7th days) and on 1st day of recovery period.

We examined central hemodynamics by the method of integral rheography [7]. We calculated the following parameters: stroke and cardiac indexes (SI and CI), total peripheral resistance (TPR) and heart rate (HR). The integral rheogram of the body was recorded before the start of WI, at the end of the 1st, 3d, 5th and 7th days of WI, as well as on the 1st and 2d days of the recovery period. We used a Soviet-made rheographic attachment, 4RG-1m, connected to an automatic recorder to obtain the rheograms. All rheogram parameters were processed individually for each subject. Student's t criterion was used for statistical processing of BP parameters. A programmable calculator was used for primary processing of rheograms, subsequent calculations and statistics.

## Results and Discussion

The subjective reactions of subjects to WI were the same. There was some nasal congestion and some difficulty in inspiration. By the end of the 1st day, pain appeared in the lumbar region, which was related to relaxation of dorsal extensors. As a rule all of the complaints disappeared by the end of the 3d and start of the 4th day, and the last days of WI were tolerated well by the subjects.

MBP was higher in the main group than controls in all observation periods (background, WI, recovery) ( $P < 0.01$ ). Minimum mean background MBP was

88.69±2.02 mm Hg and maximum 94.58±1.45 mm Hg in the main group. Base values for MBP were approximately the same in the control group--83.20±0.98 and 82.33±0.75 mm Hg. Further dynamics of MBP calculated as percentage of background value are illustrated in Figure 1. As can be seen from the diagram, MBP reaction varied during WI: 4 and 7% drop of MBP ( $P<0.01$ ) was found in 2 subjects of the main group, whereas a 4% rise was demonstrated ( $P<0.01$ ) in subjects B-ov and A-ov. In the control group, MBP dropped by a mean of 2.5% ( $P<0.01$ ).

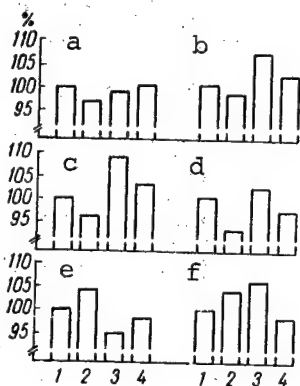


Figure 1.

Dynamics of mean BP

- 1) background MBP
- 2) mean MBP for 7 days of immersion
- 3,4) MBP on 1st and 2d recovery days, respectively

Here and in Figures 2 and 3:

- a, b) control group, subjects F-in and K-ev
- c-f) main group, subjects S-ov, M-ov, B-ov and A-ov

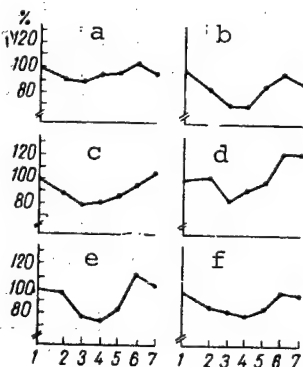


Figure 3.

Dynamics of SI

- 1) background values
- 2-5) 1st, 3d, 5th and 7th days of WI, respectively
- 6,7) 1st and 2d recovery days

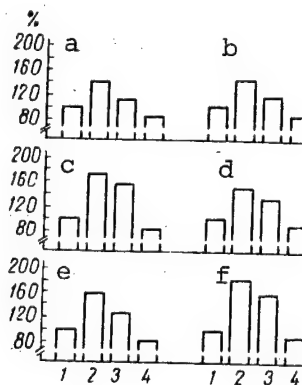


Figure 2.

Dynamics of CVP

- 1) background CVP
- 2,3) 3d and 7th days of WI
- 4) 1st day of recovery period

On the 1st day of recovery there was elevation of BP, the level of which exceeded the base value. Elevation of BP was reliable in all subjects ( $P<0.01$ ) with the exception of B-ov, whose BP dropped by 9% on the 1st day, as compared to mean value during WI ( $P<0.01$ ). BP was restored to the base level in all subjects on the 2d day of the recovery period.

Table 1 lists differences in BP reactions as assessed by comparing the CC.

In the background studies, minimal fluctuations of MBP were demonstrated in the control group. The subjects in the main group presented a wide scatter of BP values, which reached significant levels in some subjects (CC = 7.56%).

During WI, CC increased by about 4.82% in the control group and 7.31% in the main group. The 1st day of the recovery period

led to dissimilar BP responses, whereas on the 2d day of recovery there was decline of CC in both groups of subjects (Table 2). Such dynamics of dispersion during the recovery period indicates that the 1st day after WI is the time when the main processes of functional adjustment to ordinary conditions take place. It should be noted that BP fluctuations in both groups were in different ranges, i.e., maximum BP in the control group exceeded insignificantly the minimum arterial pressure of subjects in the main group. In the latter group, maximum BP repeatedly exceeded 140/90 mm Hg, which is indicative of BAH in the main group. BP exceeded this value in the main group in an average of 14% of the cases. There were no hypertensive responses in the control group.

Table 1.  
Dynamics of coefficient of covariation  
of mean dynamic blood pressure, %

| Group   | Subject | Back-<br>grnd | WI    | Recovery<br>day |      |
|---------|---------|---------------|-------|-----------------|------|
|         |         |               |       | 1               | 2    |
| Control | F-in    | 3,71          | 4,42  | 7,63            | 1,49 |
|         | K-ev    | 2,90          | 5,21  | 4,87            | 2,43 |
| Main    | S-ov    | 5,40          | 5,99  | 12,34           | 4,44 |
|         | M-ov    | 4,04          | 4,83  | 8,22            | 5,01 |
|         | B-ov    | 7,56          | 8,11  | 6,73            | 2,28 |
|         | A-ov    | 5,80          | 10,30 | 5,09            | 3,76 |

Table 2.  
Dynamics of total peripheral re-  
sistance ( $\text{dyne} \cdot \text{s} \cdot \text{cm}^{-5}$ )

| Group   | Sub-<br>jects | Back-<br>ground | WI         | Recovery<br>period |
|---------|---------------|-----------------|------------|--------------------|
| Control | F-in          | 1122 ± 46       | 1226 ± 51  | 1038 ± 50          |
| Main    | K-ev          | 1032 ± 65       | 1286 ± 78  | 1029 ± 101         |
|         | S-ov          | 960 ± 55        | 1083 ± 98  | 1002 ± 76          |
|         | M-ov          | 1310 ± 62       | 1321 ± 84  | 1100 ± 103         |
|         | B-ov          | 1345 ± 92       | 1791 ± 101 | 1307 ± 87          |

Analysis of the dynamics of MBP revealed that WI is a powerful factor that leads to functional alteration of the cardiovascular system. Identical loads led to different MBP responses in the control and main groups (see Figure 1). There were also differences between subjects in the main group, where two men presented the same tendency as the control group, while the other two presented elevated MBP during WI and a different reaction in the recovery period. Evidently, such differences in MBP dynamics are related to the fact that, in subjects S-ov and M-ov, the functional disorders of the cardiovascular system, which built up with age, did not acquire the nature of an irreversible process and the compensatory reserves of the body provided an adequate BP response to WI. In the other two members of the main group, we observed BP elevation to 150/100-160/110 mm Hg during WI, which is indicative of significant impairment of mechanisms that control vascular tonus; we could even state that these subjects suffered from the early stage of essential hypertension. It should also be noted that these individuals subjectively reported poorer tolerance to WI than the other two in the main group.

With reference to the other component characterizing the condition of the cardiovascular system, the CVP,\* it must be noted that the dynamics of this

\*Data were kindly furnished to us by A. G. Kulikova.

parameter were the same for all subjects. As can be seen in the graphs of CVP changes (Figure 2), there was elevation of CVP during WI, and it reached a maximum by the 3d day. In this period, CVP rose by more than 50% in the main group, whereas in the control group it did not reach this level. By the 7th day of WI there was a general tendency toward normalization of CVP, and the decline was more intensive in the control group. In the recovery period, all subjects presented a drop of CVP below the background level on the 1st day followed by normalization on the 2d day.

Thus, the dynamics of CVP were similar in both groups, but the changes in this parameter were more marked in the main group of subjects.

During this period of the study, HR was relatively stable, which enabled us to assess central hemodynamics using two parameters, SI and TPR. On the whole, SI changes in response to WI were the same in all subjects (Figure 3). The first days of WI were characterized by decline of SI, and this parameter had minimal values on the 3d and 5th days of WI. Maximum decline of SI did not exceed 30% of the base level. In the second half of the WI period, there was a tendency toward increase of SI and its approximation to base values. We found two types of SI reactions to the return to gravity in the recovery period. On the 1st day, SI of 3 subjects retained a tendency toward returning to the base level, after which it became stabilized at its former level. In the other subjects, SI increased on the 1st day of the recovery period and exceeded the value recorded before WI. This parameter declined on the following day, coming close to the base level. TPR (see Table 2) increased during WI in all subjects ( $P < 0.01$ ). The reaction was similar, but its elements varied. While the increase in TPR occurred in subjects B-ov and A-ov as a result of elevation of MBP, the main cause in the other subjects was a decrease in systolic output of the heart. The absence of significant differences between the main and control groups with respect to SI reaction to WI suggests that the body's hemodynamic response to WI is a common reaction that is not related to either age or functional disturbances of the cardiovascular system that one finds in older people.

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## SURVEY

UDC: 612.015.348:547.915]-06:612.766.2

### LIPID HYDROLYSIS IN MAN DURING ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 15 Jul 83) pp 40-44

[Article by I. L. Medkova, N. M. Nikolayeva and O. V. Zhiznevskaya]

[English abstract from source] Using present-day techniques, we measured the activity of pancreatic lipase in the serum and duodenal juice, the activity of monoglyceride lipase in the duodenal juice, the concentration of lipoproteins in the bile, the activity of intestinal enzymes (monoglyceride lipase and alkaline phosphatase) and the concentration of lipid fractions in the feces. These parameters were determined in six test subjects who were exposed to head-down tilt ( $-4.5^\circ$ ) for 120 days. Our findings suggest that bed rest decreases lipolytic enzymes in the duodenal juice and increases pancreatic lipase in the serum. The exposure also leads to a decrease of lipoproteins in the bile, rearrangement of the lipolytic enzymes in the intestine, and to an increase of mono-, di- and triglycerides in the feces. Our results are indicative of changes in the pancreatic function and in lipid hydrolysis and absorption. They can be interpreted as compensatory-adaptive processes of the digestive organs.

[Text] Investigation of digestive enzymes that hydrolyze lipids in the gastrointestinal tract is important, from both the standpoint of further deepening studies of the function of the digestive system and in connection with the numerous data in the literature concerning changes in lipid metabolism under the influence of extreme factors, in particular, spaceflights and hypokinesia [8, 9].

We have tried here, using modern methodological procedures, to make a combined study of the activity of some lipolytic enzymes that hydrolyze alimentary fats in both the digestive tube and on epitheliocyte membranes. We also investigated liver secretion of the main complex bile compound, which has a direct bearing on hydrolysis of lipids. In addition, we identified the lipid spectrum of feces, which partially characterizes the process of lipid utilization and condition of the digestive-transport conveyor of lipids.

Activity of lipolytic enzymes and other parameters of the process of hydrolysis of lipids had been investigated previously on man and in animal experiments with use of various extreme factors [10]. It was established that serum pancreatic lipase activity increases under hypokinetic conditions and that the level of this enzyme in pancreatic tissue drops. Redistribution of activity of intestinal lipases was observed, in the direction of increased enzyme activity in the distal segments of the small intestinal mucosa [7].

We investigated here the following parameters of the process of lipid hydrolysis in the digestive system: 1) pancreatic lipase--the most important lipolytic enzyme produced by the exocrine system of the pancreas, which has maximum activity with respect to long-chain triglycerides. This enzyme effects primarily the early stages of lipid hydrolysis in the small intestine; 2) monoglyceride lipase--lipolytic enzyme that hydrolyzes monoglycerides and effects the final process of lipid breakdown to glycerin and fatty acids; 3) alkaline phosphatase, which can also be classified as an enzyme that is instrumental in digestion of lipids. The substrate for it is referable to intermediate products of phospholipid hydrolysis. The lipid complex of bile plays an important part in processes of emulsifying lipid, as well as transfer and absorption of products of its dissociation. It includes bile acids, phospholipids, cholesterol, fatty acids, a certain amount of protein, and it characterizes the synthetic function of liver cells; 4) lipid spectrum of feces, in this case, fractions of total lipids, mono-, di- and triglycerides, which reflects the efficiency of lipid hydrolysis, furnishing information about the final products of lipid digestion.

#### Methods

This study was conducted on 6 men who spent 120 days under antiorthostatic hypokinetic (AOH) conditions with the head end of the bed tilted to  $-4.5^\circ$ .

Exocrine function of the pancreas was evaluated according to enzyme activity in batch A of duodenal contents; bile-producing function of the liver was tested by assaying lipoprotein complex content in batches B and C of duodenal juice [6] collected by duodenal catheterization after using 33%  $\text{MgSO}_4$  solution as a stimulator. Activity of pancreatic lipase in intestinal juice (batch A), blood serum and urine was measured by the method of I. L. Medkova et al. [4]. Monoglyceride lipase activity was tested in duodenal juice and feces [5]. The lipid spectrum of feces (mono-, di- and triglycerides and total lipids) was identified by thin-layer chromatography followed by densitometry in the presence of standards [2].

#### Results and Discussion

Activity of pancreatic lipase in duodenal juice underwent the following changes during hypokinesia. By the 20th day of AOH it dropped by 30%, as compared to the baseline, on the 67th day, to almost one-half, on the 89th day of hypokinesia its activity constituted only 5% of background value ( $P < 0.001$ ) and on the 112th day, 11% ( $P < 0.001$ ). The 10th day of the recovery period was characterized, as before, by reliable decline in activity of pancreatic lipase (5.5% of base value; Table 1).

Table 1. Activity of pancreatic lipase and monoglyceride lipase in duodenal juice (in  $\mu\text{mol}/\text{min}/\ell$ ;  $n = 5$ ),  $M \pm m$

| Parameter            | Back-ground       | Hypokinesia, days                 |                                   |                                 |                                 | Recovery period, 10th day       |
|----------------------|-------------------|-----------------------------------|-----------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                      |                   | 20                                | 68                                | 89                              | 110                             |                                 |
| Pancreatic lipase    | 63 900 $\pm$ 9800 | 45 300 $\pm$ 15 000<br>( $>0,1$ ) | 36 500 $\pm$ 11 200<br>( $>0,1$ ) | 3300 $\pm$ 1000<br>( $<0,001$ ) | 6900 $\pm$ 2000<br>( $<0,001$ ) | 3600 $\pm$ 1100<br>( $<0,001$ ) |
| Monoglyceride lipase | 2 600 $\pm$ 600   | 5 900 $\pm$ 1 700<br>( $>0,1$ )   | 3 400 $\pm$ 1 000<br>( $>0,1$ )   | 300 $\pm$ 90<br>( $<0,01$ )     | 160 $\pm$ 40<br>( $<0,01$ )     | 700 $\pm$ 200<br>( $<0,02$ )    |

Note: Here and in Tables 2 and 3, P is given in parentheses.

Examination of the dynamics of changes in activity of serum pancreatic lipase revealed differences in parameters of this enzyme in different subjects, and for this reason we deemed it desirable to submit the individual fluctuations in activity of this enzyme at the different tested times. In 3 subjects, blood lipase activity began to rise toward the last stage of hypokinesia (70th-112th days). On the 7th day of the recovery period, it was still high, but by the 25th day of the recovery period activity of pancreatic lipase did not exceed the normal range in these subjects. In 2 other subjects, an increase in activity of this enzyme was found only once over the entire period of the study. Rather prolonged elevation (from the 28th to 112th days) of lipase activity was demonstrated in 1 case. This parameter gradually reverted to the base value in the recovery period. Thus, from the submitted data it is apparent that blood serum pancreatic lipase activity increased in 4 out of 6 subjects during 120-day AOH: toward the end of hypokinesia in 3 cases and throughout the test period in 1. Urine pancreatic lipase level changed insignificantly during hypokinesia, with the exception of the 70th day, when it was reliably elevated.

Monoglyceride lipase activity changed in the course of the study, its activity in juice rose up to the middle of the hypokinetic period: by more than 2 times on the 20th day and by 30% on the 67th. However, with increase in duration of AOH, activity of monoglyceride lipase began to decline, and it constituted only 12% of the base level by the 88th day ( $P < 0.001$ ) and 6% by the 112th day ( $P < 0.01$ ). Activity of this enzyme remained reliably low on the 10th day of the recovery period (see Table 1). There were some fluctuations in activity of monoglyceride lipase in feces during hypokinesia: significant and reliable increase in activity was noted on the 25th, 75th and 120th days of AOH and in the recovery period (Table 2).

In our study of the lipid spectrum of feces, we were impressed by the increase in concentrations of mono- and diglycerides from the 39th to 86th days, whereas triglyceride content increased twice during hypokinesia, but changed reliably only on the 50th day. Total lipid content of feces changed insignificantly and mainly in the direction of decline toward the end of hypokinesia.

Table 2. Activity of monoglyceride lipase and alkaline phosphatase in feces ( $n = 6$ ),  $M \pm m$

| Parameter            | Base-line       | Hypokinesia, days              |                               |                                |                                |                               |                               |                               | Recov. period, 8th day         |
|----------------------|-----------------|--------------------------------|-------------------------------|--------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------|
|                      |                 | 10                             | 25                            | 39                             | 50                             | 75                            | 86                            | 120                           |                                |
| Monoglyceride lipase | $0.15 \pm 0.04$ | $0.16 \pm 0.04$<br>( $< 0.1$ ) | $1.3 \pm 0.4$<br>( $< 0.02$ ) | $0.12 \pm 0.03$<br>( $< 0.1$ ) | $0.14 \pm 0.02$<br>( $< 0.1$ ) | $1.3 \pm 0.3$<br>( $< 0.01$ ) | —                             | $1.7 \pm 0.4$<br>( $< 0.01$ ) | $0.6 \pm 0.1$<br>( $< 0.002$ ) |
| Alkaline phosphatase | $2.1 \pm 0.3$   | $1.5 \pm 0.2$<br>( $< 0.1$ )   | $1.8 \pm 0.2$<br>( $< 0.1$ )  | $2.6 \pm 0.3$<br>( $< 0.1$ )   | $2.3 \pm 0.5$<br>( $< 0.1$ )   | $2.8 \pm 0.8$<br>( $< 0.1$ )  | $3.1 \pm 0.4$<br>( $< 0.05$ ) | $4.4 \pm 0.5$<br>( $< 0.01$ ) | $1.3 \pm 0.12$<br>( $< 0.05$ ) |

Examination of alkaline phosphatase activity in feces revealed changes only toward the end of the hypokinetic period (86th and 120th days) and in the recovery period, with increased activity on the 120th day of AOH and 8th day of the recovery period (see Table 2).

Table 3.  
Concentration of lipid complex of bile (mg%) in B and C batches of duodenal contents ( $n = 5$ ),  $M \pm m$

| Batch of duodenal content | Base-line        | Hypokinesia, day                 |                                  | Recov. period, 10th day         |
|---------------------------|------------------|----------------------------------|----------------------------------|---------------------------------|
|                           |                  | 89                               | 112                              |                                 |
| B                         | $354.5 \pm 65.2$ | $296.9 \pm 22.2$<br>( $< 0.1$ )  | $298.2 \pm 50.2$<br>( $< 0.1$ )  | $418.7 \pm 59.6$<br>( $< 0.1$ ) |
| C                         | $279.9 \pm 53.1$ | $115.5 \pm 26.4$<br>( $< 0.05$ ) | $128.1 \pm 20.6$<br>( $< 0.05$ ) | $176.4 \pm 45.0$<br>( $< 0.1$ ) |

As shown by the results of the studies, there was gradual decrease in concentration of the lipid complex in batches B and C of duodenal contents during hypokinesia, but reliable changes were noted only in batch C. The concentration of lipid complex in batch B was above the base level in the recovery period, whereas batch C remained substantially lower than the background level (Table 3).

Thus, our findings indicate that exocrine function of the pancreas undergoes certain changes during 120-day bedrest. On the one hand, there is drastic decline in activity

of pancreatic lipase in duodenal juice toward the end of AOH; on the other hand, there is development of the phenomenon of "digression" of the enzyme into blood (hyperlipasemia). This is indicative of change in lipolytic processes in the gastrointestinal tract, into which lipase with diminished activity passes and, consequently, it cannot provide for completely efficient hydrolysis of fats. Apparently, the decrease in concentration of bile lipid complex in batches B and C of duodenal contents also led to worsening of conditions for lipid hydrolysis. Also, the fact that the most significant decline of this parameter was demonstrated in batch C is indicative of impairment of synthetic function of the liver, since this batch contains chiefly bile flowing from the hepatic ducts.

Analysis of intestinal digestion of lipids under hypokinetic conditions enables us to demonstrate that there is some compensatory increase in activity of monoglyceride lipase against the background of progressive decline of pancreatic lipase at the early stage of hypokinesia. Thereafter, monoglyceride lipase

activity diminished in intestinal juice, while it was above the baseline in feces, which is apparently indicative of activation of the enzyme in distal parts of the intestine, reflecting development there of compensatory and adaptive reactions in order to correct the drastically reduced activity of lipolytic enzymes in the duodenum. Under these conditions, the increase in alkaline phosphatase activity should apparently also be interpreted as a process aimed at optimizing conditions for lipid hydrolysis and transport. On the other hand, with reference to causes of increased alkaline phosphatase activity, one cannot fail to consider changes in microbial cenosis of the intestine under hypokinetic conditions, which could lead to increase in activity of this enzyme [3].

With respect to levels of end products of lipid hydrolysis in feces, we were impressed by the tendency toward increase in amount of nonlysed triglycerides.

Thus, the described findings indicate conclusively that there is worsening of conditions for digestion of lipids in the gastrointestinal tract, and one could have expected development of steatorrhea toward the end of the hypokinetic period. However, we failed to demonstrate increased elimination of lipids in feces throughout the investigation. According to data in the literature [1], steatorrhea usually develops when there is drastic decline, to 5-10% of base value, in activity of pancreatic lipase, which splits lipids in the gastrointestinal tract. In our study, there was drastic decline in activity of pancreatic lipase toward the end of the hypokinetic period, but steatorrhea was not demonstrable. This is apparently related to the fact that we studied the base level of pancreatic lipase activity. In all likelihood, when there is stimulation (intake of food) the functional capacities of the gland are still high enough to produce secretions capable of hydrolyzing enough lipids not to cause steatorrhea. In addition, membrane lipolytic enzymes, which have a tendency toward increase under AOH conditions, are instrumental in lipid hydrolysis. In this sense, the term, "compensated lipolytic insufficiency," which we use to describe exocrine function of the pancreas under hypokinetic conditions, is understandable.

It is apparent from the data submitted above that hypokinesia lowers the activity of lipolytic enzymes in duodenal juice. In the recovery period, pancreatic lipase and monoglyceride lipase levels remained reliably low, which is indicative of appreciable functional changes in the pancreas. The decline of lipolytic enzyme activity in duodenal juice was associated with increase of their activity in blood serum. This "digression" phenomenon into blood was demonstrable to a greater extent toward the end of the hypokinetic period and characterized enzymopathy. Thus, the demonstrated changes in exocrine function of the pancreas during 120-day hypokinesia are consistent with the concept of development of compensated lipolytic insufficiency. The increase in levels of mono-, di- and triglycerides in feces is also indicative of changes in hydrolysis and absorption of lipids. Moreover, the demonstrated drop in lipoprotein complex level in bile could have a negative effect on function of the hydrolytic-transport conveyer of lipids under hypokinetic conditions. Apparently the changes in lipolytic spectrum of gastrointestinal tract enzymes are indicative of development of compensatory and adaptive processes in the system of digestive organs under hypokinetic conditions for the purpose of optimizing conditions for hydrolysis

and transport of lipids. This is confirmed by the increase in activity of monoglyceride lipase and alkaline phosphatase in feces.

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## DISSOCIATION OF AUTONOMIC AND SENSORY VESTIBULAR REACTIONS

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[Article by Yu. V. Krylov, O. A. Vorob'yev and V. V. Zaritskiy]

[English abstract from source] The studies of healthy people and test subjects with vestibular reception disorders yielded data about relative independence of the vestibulo-autonomic and vestibulo-sensory reactions during routine vestibulometric and tilt tests. The subjects with a changed labyrinthine function showed a higher vestibulo-autonomic stability as compared to those with normal hearing. In both groups the sensory component of vestibular reactions did not differ significantly. Hemodynamic changes were found to modify some parameters of the nystagmic reactions.

[Text] Many authors have pursued comparative studies of healthy and deaf-mute subjects who had changes in both the auditory and nonauditory part of the labyrinth in order to investigate the role of vestibular reception in development of a set of vestibular reactions. Kreidl [20] and Polak [22] had already observed that deaf-mutes tolerate vestibular stimulation better, and they attributed this to absence of vestibular function. S. N. Khechinashvili [11-12], S. S. Markaryan [9] and a number of other researchers demonstrated experimentally that deaf-mutes deprived of vestibular function do not react to angular and linear accelerations. Neither nystagmus nor disequilibrium could be elicited in them with use of galvanic stimulation of the labyrinths. It was shown that spatial orientation is impaired in deaf-mutes [2, 4].

However, several studies [1, 9, 15, 23] demonstrated that among deaf-mutes there are some with functional and some with nonfunctional vestibular systems. Reports on the incidence of functional vestibular impairment in deaf-mutes are contradictory. Thus, vestibular reactions were absent in 14-23% of those tested according to Goldstein [15] and Preibisch-Effenberger [23], and in 70% according to Jakobi [19].

Recently the opinion has been voiced that changes occur during spaceflights in vestibular function under the influence of weightlessness, which leads to depression of afferentation from otolith receptors [7, 17]. This, perhaps,

impairs interaction between analyzer systems ("sensory conflict") that plays an important part, in the opinion of some authors [6, 18], in the genesis of space motion sickness. Moreover, such factors as redistribution of body fluids in a cranial direction [5, 21], reduced load on mechanoreceptors of the human body and others may apparently be involved in development of this adverse group of symptoms in weightlessness.

The experience of manned spaceflights revealed that autonomic manifestations are observed in the acute period of adaptation to weightlessness on the average in 40% of the participants, whereas sensory disturbances in the form of brief spatial illusions were reported by virtually all members of space missions [14, 16]. This shows that there is relative independence of autonomic and sensory reactions that arise upon stimulation of the vestibular analyzer combined with stimulation of other sensory systems in weightlessness.

Our objective here was to investigate the nature of autonomic vestibular, nystagmic and sensory vestibular reactions of individuals with altered labyrinthine function (loss of hearing), as compared to subjects with normal hearing using traditional methods of vestibulometry and in antiorthostatic position (AOP), i.e., with simulation of some of the physiological effects of weightlessness on man.

#### Methods

At the first stage, vestibular analyzer function was tested using traditional methods. Binaural cold calorization was performed with water at a temperature of 30°C in a volume of 300 ml for 40 s; we alternately irrigated the right and left external auditory meatus. The subject was in supine position with the head elevated at an angle of 30°.

Adequate vestibular stimulation, with the subject in seated position, was delivered in a portable electric revolving chair. We used rotation on a trapezoid program with angular velocity of 180°/s and accelerations of  $\pm 90^\circ/\text{s}^2$ , and the test with continuous build-up of Coriolis accelerations (CVCA) [9].

Vestibular stimulation in AOP was delivered on a special turntable equipped with a platform to rotate the subject in supine position. The axis of rotation passed through the subject's head. We used rotation on a trapezoid program ( $60^\circ/\text{s}$ ,  $\pm 40^\circ/\text{s}^2$ ), undamped sinusoid rotation with a 5-s half-cycle and maximum velocity of rotation of  $60^\circ/\text{s}$  and the test with exposure to Coriolis accelerations. The latter was performed while rotating the stand at the rate of  $120^\circ/\text{s}$  with the head moving in a sagittal plane with  $\pm 30^\circ$  amplitude of deviation from the human median axis and half-cycle of 4 s. We started vestibular stimulation 15 min after moving the subject to AOP, the angle of which was determined individually ( $10$ – $15^\circ$ ) for each subject on the basis of arteriovenous pulsograms (AVP) recorded from a vascular fascicle on the neck [13], which enabled us to effect continuous monitoring of level of blood redistributed to the head.

During all types of vestibular stimulation (which was delivered with the subject's eyes closed) we recorded horizontal nystagmus by means of electro-nystagmography [8]. Coefficient Ka of asymmetry of parameters of nystagmus

was determined using the formula  $Ka = \frac{R - L}{R + L} 100\%$ , where R and L are the tested parameters of nystagmus directed toward the right and left, respectively.

Resistance to motion sickness was evaluated according to time of endurance of tests with use of Coriolis accelerations before distinct nausea appeared. The vestibulosensory reaction was assessed according to duration of illusion of counterrotation and severity of "rocking" illusion during CVCA test, which were recorded according to the subject's report.

Two groups of subjects participated in the study: individuals 17-20 years of age with altered labyrinthine function (main group, 72 people), among whom we selected 26 physically healthy volunteers for rotation stimulation in seated position and 5 in AOP; individuals 18-22 years of age with normal labyrinthine function who had undergone examinations by an otorhinolaryngologist and neurologist (control group), 50 of whom were rotated in seated position and 6 were submitted to vestibular stimulation in AOP. We first performed tonal threshold audiometry using a portable audiometer on subjects in the main group, in order to determine the severity of hearing impairment.

The findings were submitted to statistical processing with use of criteria of reliability of differences of Student (t) and Wilcoxon-Mann-Whitney (U).

## Results and Discussion

Analysis of the results of audiometry on the main group of subjects revealed that, according to the classification of L. V. Neyman [10], 97% presented deafness--average loss of hearing exceeded 80 dB in the frequency ranges of 500, 1000, 2000 and 4000 Hz, and the rest (3%) had grade III hearing impairment at the same frequencies in the range of 70 to 80 dB.

Table 1 summarizes the results of determining severity of cold caloric nystagmus in the subjects.

Table 1. Parameters of cold caloric nystagmus (M±m)

| Group of subjects | Time, s                 | Total beats              | Frequency I/s         | Overall amplitude degrees | Mean amplit. degrees  | RSP, °/s                |
|-------------------|-------------------------|--------------------------|-----------------------|---------------------------|-----------------------|-------------------------|
| Main              |                         |                          |                       |                           |                       |                         |
| R                 | 157,5±12,1              | 344,5±35,9               | 3,0±0,1               | 320,3±69,7                | 5,5±1,3               | 40,2±6,8                |
| L                 | 147,5±21,8<br>(6,7±1,8) | 302,5±68,7<br>(10,4±6,5) | 2,6±0,4<br>(9,3±3,4)  | 279,5±113,3<br>(20,2±4,4) | 5,1±1,6<br>(12,3±4,7) | 31,5±5,8<br>(20,0±4,9)  |
| Control           |                         |                          |                       |                           |                       |                         |
| R                 | 133,3±6,3               | 253,9±20,2               | 2,35±0,11             | 454,9±46,5                | 9,9±1,0               | 34,4±3,4                |
| L                 | 140,5±9,5<br>(6,6±1,3)  | 264,1±25,9<br>(4,7±1,2)  | 2,27±0,7<br>(4,9±0,7) | 457,4±34,9<br>(7,7±1,3*)  | 10,3±0,7<br>(6,1±1,0) | 32,5±2,2<br>(10,4±1,9*) |

Note: L--nystagmus to the right, L--to the left. Asterisk indicates  $P < 0.05$ . Here and in Table 2, coefficient of asymmetry is given in parentheses.

It was established that asymmetry of overall amplitude and rate of slow phase (RSP) of nystagmus in the main group of subjects differed reliably from the control. Consequently, in this group of subjects deafness was associated with impairment of vestibular function, since vestibular asymmetry with the caloric test is considered to be one of the most important indicators of damage to the nonauditory part of the labyrinth [3].

Comparative analysis of postrotatory nystagmus (Table 2) indicates that the amplitude parameters and RSP were reliably lower with rotatory stimulation in the main group of subjects than the control group. Deaf subjects presented marked asymmetry in number of beats and frequency of nystagmus, which is also indicative of involvement of the vestibular part of the labyrinth.

Table 2. Parameters of postrotation nystagmus

| Group of subjects | Duration, s               | Beats                    | Freq., I/s              | Overall amplitude degrees  | Mean amplit. degrees     | RSP, °/s                   |
|-------------------|---------------------------|--------------------------|-------------------------|----------------------------|--------------------------|----------------------------|
| Main              |                           |                          |                         |                            |                          |                            |
| R                 | 36.2±1.96                 | 65.6±4.41                | 2.6±0.14                | 254.7±17.45                | 9.7±0.75                 | 17.9±1.56                  |
| L                 | 37.3±1.84<br>(13.38±1.86) | 64.5±5.8<br>(18.02±2.49) | 2.5±0.6<br>(12.1±1.78*) | 216.7±26.0<br>(13.23±2.9)  | 8.82±0.9<br>(15.65±2.31) | 14.31±1.49<br>(13.53±3.24) |
| Control           |                           |                          |                         |                            |                          |                            |
| R                 | 37.6±1.0                  | 76.6±3.0                 | 3.0±0.1                 | 731.6±72.2**               | 10.4±0.8                 | 60.4±2.5**                 |
| L                 | 37.2±0.8<br>(11.3±0.9)    | 71.3±2.3<br>(11.6±0.8*)  | 2.9±0.1<br>(7.0±0.5*)   | 589.8±58.8**<br>(14.8±1.1) | 16.8±1.4*<br>(16.2±1.3)  | 60.4±3.1**<br>(17.9±1.3)   |

Note: Here and in Table 3: R--rotation to the right, L--to the left. One asterisk-- $P < 0.05$ , two-- $P < 0.01$  (differences between parameters of main and control groups).

Illusion of counterrotation after the chair stopped lasted an average of  $16.1 \pm 3.2$  s, which is in the physiological range.

However, in spite of absence of reliable differences in sensory vestibular reactions to rotatory stimulation of the labyrinths, tolerance to CVCA constituted  $7.0 \pm 0.5$  min in the main group and  $2.4 \pm 0.4$  min in the control group of subjects of the same age. This is indicative of higher autonomic vestibular tolerance of the deaf. During the test, the latency period of appearance of rocking illusion constituted a mean of  $26.1 \pm 2.7$  s, and it was virtually the same as the sensory vestibular reaction of subjects in the control group-- $24.8 \pm 2.2$  s. Heart rate (HR) and direction of changes in arterial pressure (BP) of subjects in the main group did not exceed the physiological norm.

Thus, deaf subjects presented somewhat higher autonomic vestibular endurance than those with normal hearing, although the sensory component of vestibular reactions (illusions of counterrotation and rocking) presented no reliable differences between the two groups. This can be interpreted as some degree of dissociation of autonomic and sensory vestibular reactions during tests in seated position.

The results of testing vegetative vestibular tolerance in AOP revealed that the time for the test with use of Coriolis accelerations constituted

6.9±1.5 min in the main group and 5.8±1.0 min in control subjects, but the differences were unreliable.

Analysis of features of the nystagmic reaction in AOP (Table 3) established reliable hyporeflexia, as manifested by decline of amplitude parameters of nystagmus in the sinusoid test and in number of beats [jerks?] of post-rotation nystagmus. This may be indicative of the modifying influence of hemodynamic changes, which are observed in AOP, on vestibular function of man, although one must take into consideration the fact that when conducting tests in AOP and seated position, the rate of rotation of subjects and orientation of the semicircular canals in relation to the axis of rotation were not identical.

Table 3. Parameters of nystagmic reaction with vestibular stimulation in AOP (M±m)

| Group of subjects |   | Sinusoid rotation |                   | Postrotation nystagmus |           |
|-------------------|---|-------------------|-------------------|------------------------|-----------|
|                   |   | beats             | overall amplitude | duration, s            | beats     |
| Main              | R | 10,9±1,5          | 15,3±2,8          | 16,3±1,7               | 29,5±2,7  |
|                   | L | 9,1±1,9           | 10,8±2,2          | 29,4±4,6               | 36,8±6,3  |
| Control           | R | 11,0±1,0          | 24,6±5,2*         | 19,9±3,4               | 38,4±3,3* |
|                   | L | 10,1±0,5          | 23,5±2,4*         | 21,4±6,1               | 43,6±5,2  |

\*  $P < 0,05$ .

There were no reliable differences in duration of postrotation illusion in deaf subjects and those with normal hearing in AOP, and it constituted 10.4±3.1 s and 14.4±4.4 s, respectively.

The identical vestibular sensory reactions of both groups of subjects and somewhat different autonomic vestibular manifestations in AOP are indicative of the fact that there is relative independence of manifestations of sensory and autonomic reactions to adequate vestibular stimulation when some of the physiological effects of weightlessness are simulated by AOP.

AVP parameters, blood pressure and heart rate changed in this series of studies in the same direction in both groups, and no reliable differences were demonstrable.

Thus, the findings are indicative of relative independence of autonomic and sensory vestibular (illusions) manifestations in both traditional vestibulometric tests and with vestibular stimulation in AOP (though to a lesser extent) in individuals with impaired vestibular reception and healthy subjects. This confirms the opinion that, even with high autonomic vestibular stability, it is possible to retain a marked sensory component. This must be taken into consideration in assessing sensory manifestations that appear in flight in cosmonauts with high resistance to motion sickness.

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# INVESTIGATION OF VESTIBULAR STRUCTURE AND ION COMPOSITION OF SPUR-TOED FROG LARVAE AFTER EXPOSURE TO WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 5 Dec 83) pp 48-52

[Article by D. V. Lychakov and Ye. A. Lavrova]

[English abstract from source] Clawed frog larvae (stages 45-46) that developed for 9 and 8 days beginning with the blastula and tail bud stages, respectively, in the weightless state were investigated. Scanning microscopy of the larval labyrinths did not reveal significant qualitative changes in the receptor and supporting cells of the maculae and in the otolith membrane. Determination of the electrolyte composition (Na, K, Ca, Mg) of the larval body showed no significant changes in the relative content of these elements. The morphometric examinations indicated an increase of the size of the utricular otoliths by 1.3 times as a result of exposure to weightlessness. There was a tendency for a greater asymmetry between the left and right otoliths in the same larva.

[Text] Development of the vestibular system of amphibians in weightlessness has been studied for several years [2, 4]. In our study, in addition to traditional methods of processing material of such investigations--light microscopy (LM) and fluoroscopic electron microscopy (FEM)--we used some new ones--scanning electron microscopy (SEM), morphometry and chemical analysis. SEM is the most adequate method of studying spatial organization of the otolith membrane and receptor cell hairs, i.e., structures that are directly exposed to gravity stimuli. Morphometry was used to measure the volume of otoliths in order to assess the extent of their development in the experiment, as compared to the control. Chemical analysis techniques were used to assay Na, K, Ca and Mg in the body of larvae and in the water, in which they developed, in order to investigate formation of the composition of inorganic elements of the body in weightlessness.

## Methods

Larvae of the *Xenopus laevis* spur-toed frog developed from the blastula and caudal bud stages for 8-9 days in EMKON biocontainers [4] at a temperature of 15°C aboard the Salyut-6 orbital station. Sixteen live larvae, delivered

to the laboratory on the 2d day after landing of the descent capsule were fixed and treated by a previously described method [13] for examination with SEM and FEM. Ultrafine serial sections (10  $\mu\text{m}$  thick) were examined under an IEM-100B FEM; the internal endolymphatic surface of the labyrinth was examined under an ISM-35 SEM. Otoliths from 10 live larvae, which were also delivered on the 2d postflight day, were frozen whole in liquid propane cooled with liquid nitrogen to  $-160^{\circ}\text{C}$ , dried under vacuum at  $-40^{\circ}\text{C}$  for 3 days and imbedded in epon-812, in order to preserve as much as possible the in vivo dimensions for morphometric studies. Serial frontal sections of the labyrinth were prepared from blocks. We calculated overall area occupied by otoliths on all sections on photographs, and after multiplying it by section thickness (10  $\mu\text{m}$ ) we found the otolith volume [9].

Eight live larvae received 5 h after landing of the descent capsule were placed in preweighed quartz tubes for chemical analysis. In the laboratory, the tubes with specimens were dried to a constant mass at  $105^{\circ}\text{C}$ , we ashed them with concentrated nitric acid in an air-dry bath at  $90^{\circ}\text{C}$  for 1-2 days until organic matter was completely dissolved. The samples were diluted in distilled water, then we assayed concentrations of Na and K by flame photometry (Zeiss III) in an air-propane flame, and concentrations of Ca and Mg by atomic absorption photometry in an air-acetylene flame.

## Results and Discussion

The larvae that developed from roe, both experimental and control, were at stages 45-46 [5]. SEM examination revealed that there are 3 macular primordia, rather than 2 as previously thought [4], in the larval labyrinth. The utricular macula lies on a horizontal protuberance that divides the anterior part of the labyrinth into two halves; the saccular and lagenar macula, which is separated from the former by a narrow layer of undifferentiated cells, lie on the medial wall of the labyrinth (Figure 1). Examination of the macular surface by SEM revealed that the structure of bundles of sensory hairs, polarization of stereocilia in relation to kinocilia, stacking of cells in maculae and distribution of microvilli on the cell surface in weightlessness did not differ from control values.

In the experiment, as in the control, receptor cells can be divided into four types, according to structure of the fascicle of cilia (Figure 2). Qualitatively, the otolith membrane did not differ from the control. It must be noted that the saccular and lagenar maculae are covered with a single otolith that has not yet separated in larvae at stages 45-46. The otolith membrane consists of numerous fine crystalline otoconia welded into a gel-like layer connected to the macular surface by vilaments of the subcupular network. On the whole, the findings conform well to the results of our previous studies conducted with use of LM and FEM, where we also failed to demonstrate noticeable qualitative changes in structure of otolith organs [2, 4].

Table 1 lists the results of measuring larval otoliths. In making measurements of otolith volumes, we considered only the otoconial layer. In some larvae, the labyrinth tore during freezing, as distinctly seen under an LM. In such labyrinths, otolith volumes were not calculated due to possible

loss of otoconia. The saccular and lagenar otoliths were evaluated as a single whole by virtue of their morphological continuity. Otolith volumes vary markedly in different larvae. In the experiment, we observed an increase in average otolith volume; however, it was unreliable for the lagena-sacculus ( $t_d = 0.9 < t_{st} = 2.1, 2.7, 3.7$ ) and for the utricle otolith it was reliable with probability of 0.95 and 0.99 ( $t_d = 3.5$  and  $t_{ts} = 2.0, 2.7, 3.7$ ). The mechanism of increase in volume of utricular otolith is not clear. In general, we do not know the extent of variability of the otolith system as related to change in gravity. Lim et al. [9], who studied the labyrinth of rats submitted to centrifuging during the embryonic and postnatal periods, found some decline, but statistically unreliable, in volume of the otolith membrane of the sacculus. Unfortunately, they did not provide any data about the utricle in the cited work. The absence of an effect in the saccular-lagenar otolith of spur-toed frog larvae is apparently related to metabolic distinctions. The existing morphological and chemical data indicate that utricular and saccular otoliths, at least in mammals, differ in rate of Ca metabolism, resistance to toxic agents and in aging process [7, 8, 10, 11]. Apparently this can explain why there are differences in the reaction to weightlessness of the utricle and sacculus-lagena. We observed significant asymmetry between the dimensions of the left and right otoliths of the same larvae in both the experiment and control (see Table 1). However, larger dimensions are not inherent in a particular side. In the experiment, asymmetry was generally more marked, but with use of Student's criterion this difference was statistically unreliable. Asymmetry of otolith mass has been described for fish and is viewed as one of the causes of onset of motion sickness [6]. It is interesting to compare the distinctions of an animal's motor activity in weightlessness to the degree of asymmetry of its otolith system.

Table 1. Results of measurement of otolith volumes in spur-toed frog larvae developing for 9 days in weightlessness

| Parameter   | Utricle        |                 | Sacculus-lagena |                  |
|---|----------------|-----------------|-----------------|------------------|
|   | control        | experiment      | control         | experiment       |
| Number of larvae used   | 14             | 9               | 14              | 10               |
| Number of otoliths measured   | 22             | 14              | 22              | 16               |
| Otolith volume ( $M \pm \sigma$ ) $\cdot 10^4 \mu m^3$  | $26.3 \pm 5.3$ | $34.2 \pm 7.3$  | $146 \pm 28.3$  | $156.0 \pm 35.6$ |
| Difference in otolith volume in the same larva in relation to smaller one, % ( $M \pm \sigma$ ) | $16.5 \pm 6.2$ | $24.2 \pm 15.5$ | $14.5 \pm 9.2$  | $19.8 \pm 6.4$   |

Table 2. Proportion of alkaline and alkaline-earth metals in spur-toed frog larvae developing for 8 days in weightlessness

| Group      | Na             | K              | Ca            | Mg            |
|------------|----------------|----------------|---------------|---------------|
| Control    | $67.7 \pm 5.3$ | $21.3 \pm 2.7$ | $5.8 \pm 2.2$ | $5.0 \pm 0.9$ |
| Experiment | $67.0 \pm 4.3$ | $21.0 \pm 3.4$ | $6.8 \pm 1.7$ | $5.0 \pm 0.9$ |

Note: Total electrolytes (in meq) is taken as 100%,  $M \pm \sigma$  ( $n = 8$ ).

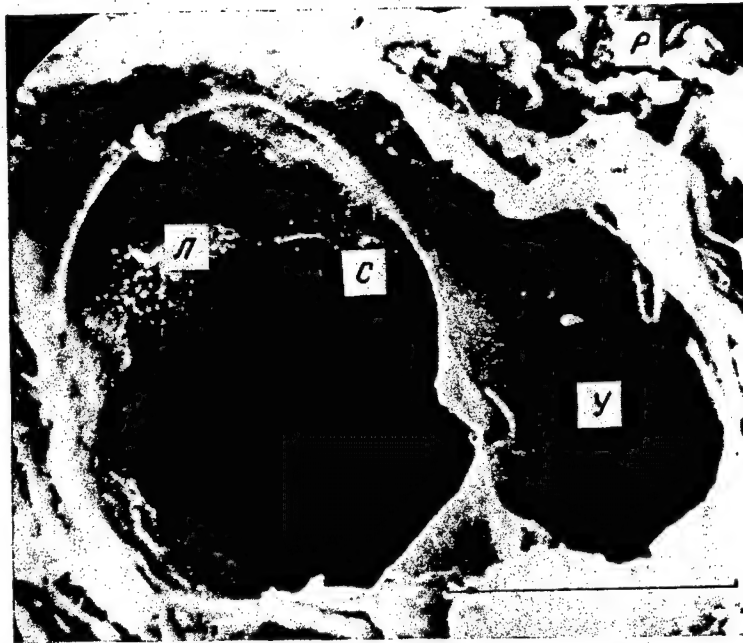


Figure 1. View from above of dissected right labyrinth from spur-toed frog larva at age of 8 days. Experiment. Scanning electron microscope. Scale 100  $\mu$ m

y) utricular macula c) saccular macula л) lagenar macula p) rostral direction

The proportion of Na and K in endolymph, presence of sufficient quantity of Ca and certain other electrolytes, including Na and Mg, are of substantial importance to normal development of otoliths [3, 4]. In view of the demonstrated enlargement of experimental otoliths, it was interesting to assess ion metabolism of larvae. However, because of the difficulty of identifying the ion composition of different parts of the developing larva, we estimated the distinctions of ion composition for the entire body. In each specimen, we measured Na, K, Ca and Mg, and considered the sum of these elements to be 100%, and the share of each element was given in milliequivalents [1]. The results of our studies revealed that ion composition of larvae developing in weightlessness did not differ from the control group (Table 2). Na was present in the largest amount among the electrolytes (67%), there was almost one-third this amount of K, while Ca and Mg content was about the same and was in the range of 5-7%. These findings are consistent with data obtained by x-ray microanalysis, which demonstrated that the qualitative distribution of Na, K, Ca, P and S in the labyrinth and eye of *Brachydanio rerio* fish fry developing in weightlessness from the stage of 5 somites for 6 days was the same as in the control [4]. However, one cannot rule out the possibility that body weight may differ with development in weightlessness from development on earth, which would be associated with a proportionate change in amounts of all electrolytes. This question can only be answered in future experiments with measurement of body mass and different liquid phases.

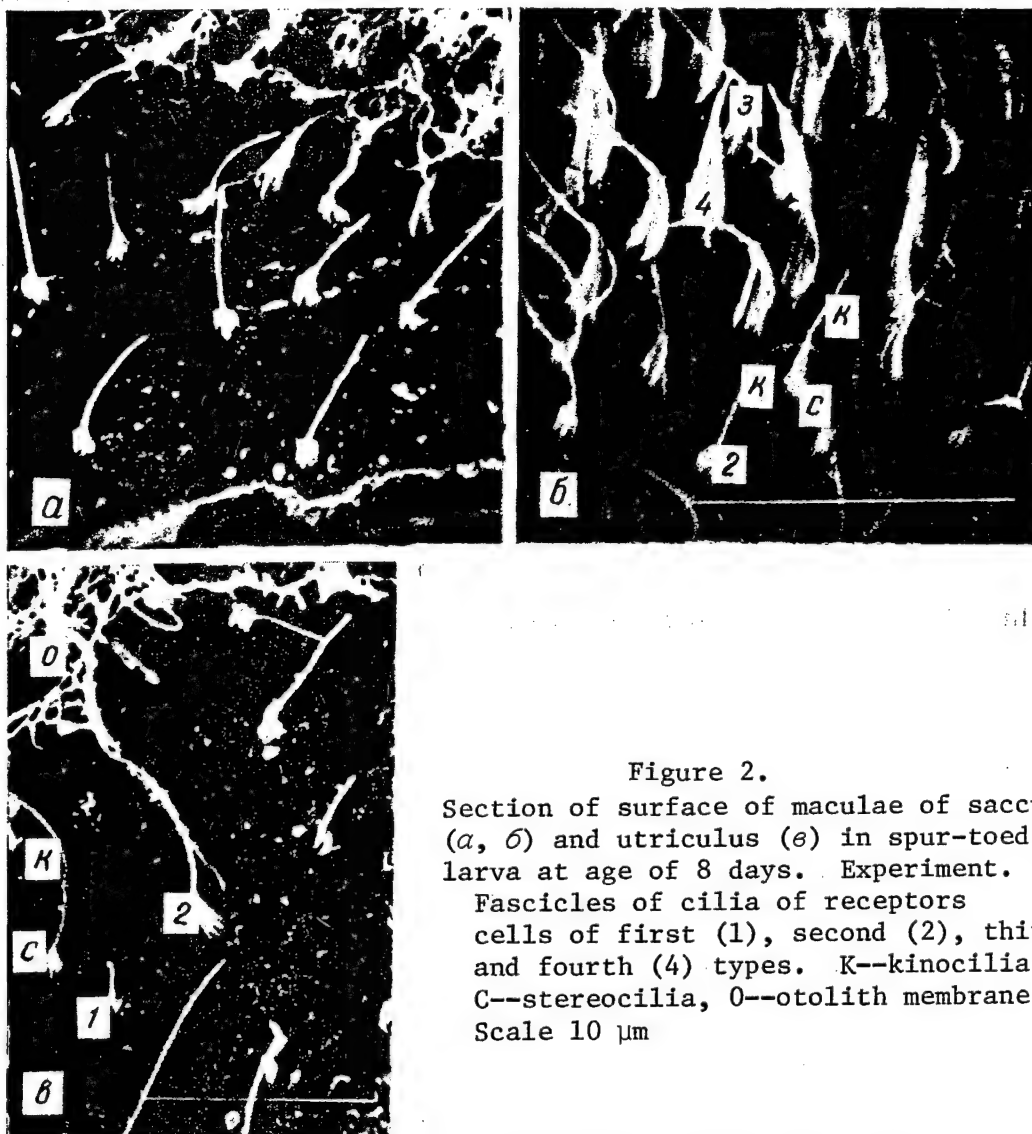


Figure 2.

Section of surface of maculae of sacculus (a, b) and utricle (c) in spur-toed frog larva at age of 8 days. Experiment. SEM.

Fascicles of cilia of receptors cells of first (1), second (2), third (3) and fourth (4) types. K--kinocilia, C--stereocilia, O--otolith membrane. Scale 10  $\mu$ m

Thus, investigation of the developing labyrinth of spur-toed frog larvae using SEM failed to demonstrate appreciable qualitative changes in organization of receptor and pillar cells of the macula and in the otolith membrane. Measurement of electrolyte composition of larvae also revealed that there were no gross changes in relative amounts of elements. However, morphometric measurements revealed 1.3-fold enlargement of utricular otoliths in weightlessness. Yet to be answered are questions of how the increase in volume is related to otolith mass, whether there is equalization of dimensions and mass of otoliths in subsequent larval development and to what extent are otoliths of vertebrates dependent on gravity.

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PAIRING PRINCIPLE AND KINEMATIC ASYMMETRY OF OTOLITH SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 4 May 84) pp 53-55

[Article by V. K. Popov and R. S. Ivanova (People's Republic of Bulgaria)]

[English abstract from source] Using a mathematical model, otolith stimulation in response to man's movements in a system rotating with a constant angular velocity was examined. Man moved his head or body forward or sideward obeying the trapezoidal rule. The resulting accelerations that acted upon the left and right otoliths were determined. The existence of two otoliths that are symmetrical relative to the sagittal plane was found to be responsible for the left-right asymmetry that accompanied movements in the rotating system, the asymmetry being most distinct during tilts to the left or to the right.

[Text] One of the probable causes of autonomic discomfort and sensory inadequacy when a man moves in a rotating system is the effect on the vestibular system of additional linear (Coriolis) and angular (precession) accelerations [3-5]. When considering this problem one should bear in mind some of the structural distinctions of the otolith system.

The otolith system is a paired organ. The utricular and saccular maculae are approximately symmetrically situated in relation to the sagittal plane, in the horizontal plane and planes parallel to the sagittal plane.

At rest (effect only of gravity) and during ordinary movements in everyday life, there is an identical effect of linear accelerations on otoliths on the right and left side (left-right symmetry).

In this regard, the question arises as to whether this symmetry of effect is retained when man moves in rotating systems.

The present work is a continuation of investigations [1, 2] dealing with this question.

Stimulation of otoliths of a subject sitting on a chair that revolves about the vertical axis at a constant angular velocity  $\omega$  and tilting his head or

trunk forward or to the side was simulated on a previously proposed [1, 2] kinematic model of otoliths. Of the three tested laws of human motion (bending at a constant angular velocity, bending according to sinusoid and trapezoid laws of change in velocity), the trapezoid was found to be closest to reality [1]. Let us analyze stimulation of otoliths when a subject bends at a velocity that changes according to the trapezoid law.

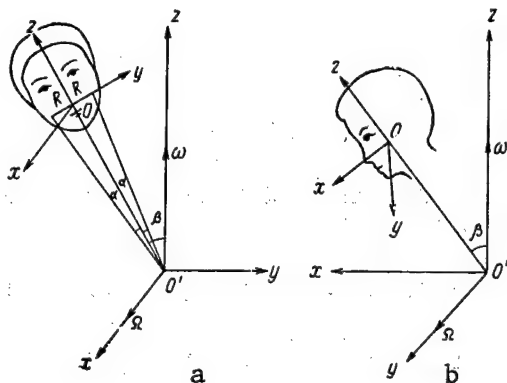


Figure 1.  
Sketch of kinematic model

a) with tilt in relation to  
O'x axis

b) with tilt in relation to  
O'y axis

Explained in the text.

Figure 1 illustrates a sketch of the kinematic model; there,  $O'xyz$  and  $OXYZ$  are systems of coordinates related to the chair and head, respectively; with  $t = 0$ ,  $OX \parallel O'x$ ,  $OY \parallel O'y$  and  $OZ \parallel O'z$ . The beginning of the system of coordinates  $O$  is situated in the middle of the line that connects the right and left otolith systems;  $OX$  is directed toward the nose and  $OY$ , to the left ear. We consider the otolith membranes to be flat structures; utricular and saccular membranes (UM and SM) on the same side are represented by one material point situated at distance  $R$  from the start of coordinates  $O$ .

We consider that SM are situated in planes that are parallel to  $XZ$  and UM, in plane  $XY$ , resultant linear accelerations acting in the plane of

the otolith membrane are adequate stimuli for otolith receptors.

Formulas were derived in [7] for resultant accelerations  $a_i (a_{xi}, a_{yi}, a_{zi})$ , ( $i = 1, 2$ ) that affect otoliths:

with tilt about axis  $O'x$  (see Figure 1a):

$$\begin{aligned} a_{xi} &= 2L\omega\Omega \cos(\beta + \alpha); \\ a_{yi} &= -g \sin \beta - L\omega^2 \sin(\beta + \alpha) \cos \beta - \\ &\quad - L \cos \alpha \pm L\Omega \sin \alpha; \\ a_{zi} &= -g \cos \beta - L\omega^2 \sin(\beta + \alpha) \sin \beta - \\ &\quad - L\Omega^2 \cos \alpha \pm L\Omega \sin \alpha; \end{aligned} \quad (1)$$

with tilt about axis  $O'y$  (see Figure 1b):

$$\begin{aligned} a_{xi} &= g \sin \beta - l\omega^2 \sin \beta \cos \beta + l\Omega; \\ a_{yi} &= \pm R\omega^2 + 2l\omega\Omega \cos \beta; \\ a_{zi} &= -g \cos \beta - l\omega^2 \sin^2 \beta - l\Omega^2, \end{aligned} \quad (2)$$

where  $\alpha$  is the angle between axis  $O'z$  and the line that connects  $O'$  with the otoliths,  $\beta$  is the angle of subject's turn about axis  $O'x$  or  $O'y$  while bending at angular velocity  $\Omega$ ,  $l$  is distance between  $O'$  and  $O$ ,  $L$  is distance

from  $O'$  to the otolith membranes. Indexes  $i = 1$  and  $i = 2$  refer to accelerations acting on the left and right otoliths, respectively.

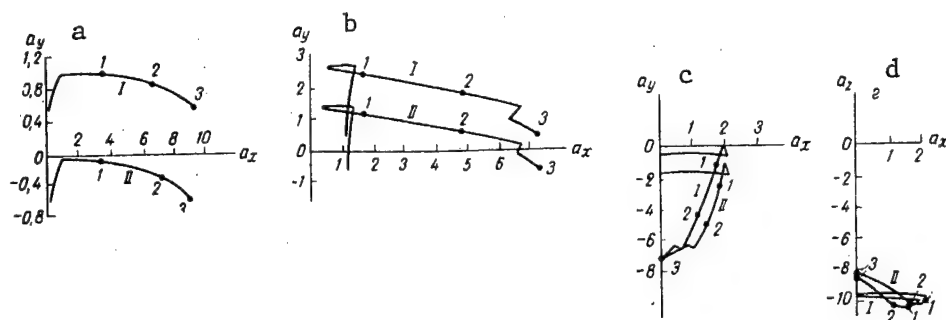


Figure 2. Hodographs of accelerations. Circled numbers refer to time (s)

In plane XY: a) with head tilted forward  
b) with trunk tilted forward  
c) with trunk tilted to the side  
In plane XZ: d) with trunk tilted to the side

I) right macula  
II) left macula

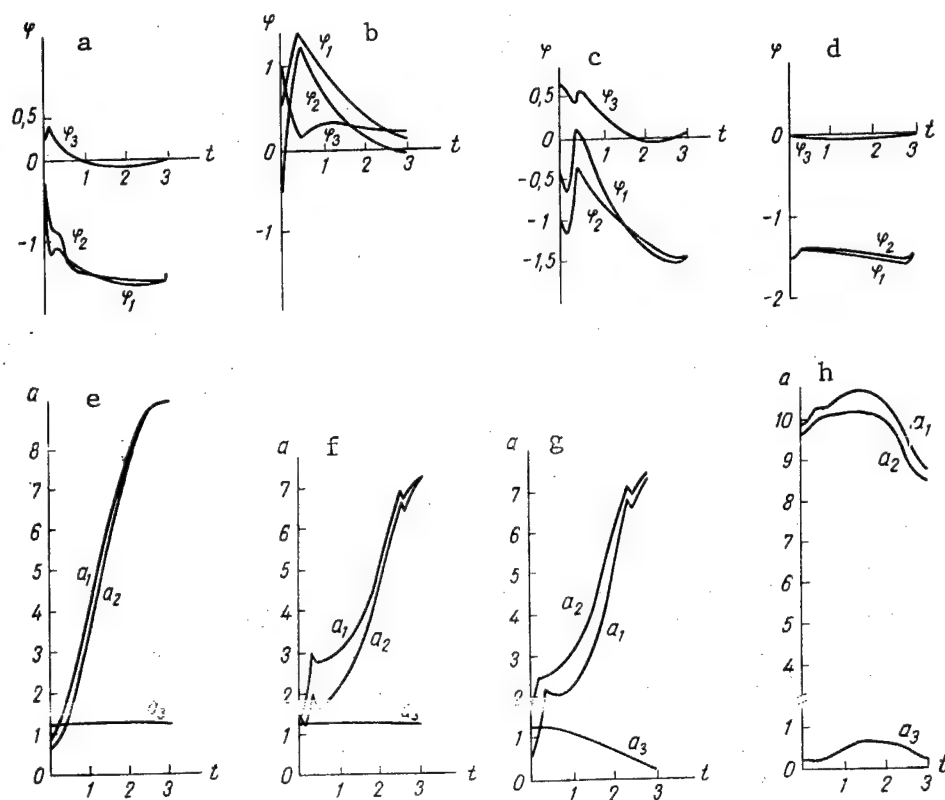


Figure 3. Curves of phases and phase differences (a, b, c, d) and dynamics of changes in moduli of vectors of asymmetry and accelerations (e, f, g, h) in cases considered in Figure 2 (a, b, c, d)

Kinematic models (1) and (2) were analyzed numerically on a computer with the following values for parameters:  $\omega = 3.14 \text{ s}^{-1}$ ; duration of tilting motion 3 s, including 0.3 s at angular acceleration  $\Omega = 5/3 \text{ s}^{-2}$ , 2.2 s at constant angular velocity  $\Omega = 0.5 \text{ s}^{-1}$  and 0.5 s with angular acceleration  $\Omega = -1 \text{ s}^{-2}$ ; angle  $\beta$  changes from  $0^\circ$  to  $75^\circ$ ;  $R = 0.06 \text{ m}$ ;  $l = 0.15 \text{ m}$  with tilting motion of head and  $l = 0.65 \text{ m}$  with tilting motion of trunk.

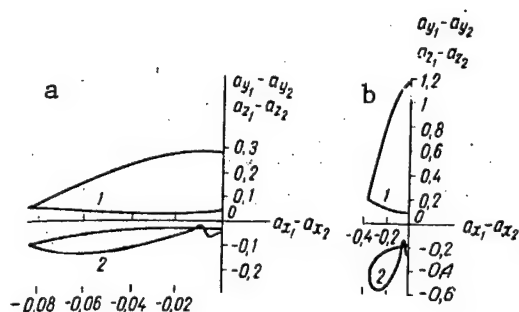


Figure 4.  
Hodographs of vectors of asymmetry  
in planes XY (1) and XZ (2)  
a) when bending head  
b) when bending trunk

As a result of numerical solution of equations (1) and (2) we obtained hodographs of resultant accelerations (Figure 2) for the left and right UM and SM during tilting motions of the head and trunk, separately for bending down ( $\beta = 0-75^\circ$ ) and straightening up ( $\beta = 75-0^\circ$ ).

The curves of phases  $\varphi_1$  and  $\varphi_2$  (angles between projections of acceleration vectors on the macular plane and axis X) and their difference  $\varphi_3$  as a function of time, as well as dynamics of change in difference in accelerations acting on the right and left otolith, the modulus of the asymmetry vector  $|a_3|$  and moduli of acceleration vectors  $|a_i|$  ( $i = 1, 2$ ) are illustrated in Figure 3.

Figure 4 illustrates hodographs of asymmetry vectors with tilting of the head and trunk.

Analysis of the obtained curves enables us to draw the following conclusions:

Resultant vectors of accelerations acting on the otoliths in 0-3 s with tilting of the head (trunk) in a rotating system have complex dynamics (abrupt changes in direction and magnitude, presence of loops on their hodographs, etc.).

The changes in vectors of resultant accelerations acting on the left and right otoliths are not synchronous and do not have coinciding phases, and as a result asymmetry appears between input effects on the right and left otoliths.

The results of these model studies revealed that presence of a right and left otolith is the cause of appearance of unusual combinations of stimuli on the left and right sides upon moving the head in a rotating system which, in turn, probably elicits inadequate reactions.

The asymmetry and distinctions of dynamics of input stimuli are more marked when the trunk is tilted than the head, as well as when tilts are made to the side, as confirmed by subjective evaluation of sensations.

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RAT SKELETAL MUSCLES WITH SIMULATION OF PHYSIOLOGICAL EFFECTS OF  
WEIGHTLESSNESS (MORPHOLOGICAL STUDY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19,  
No 3, May-Jun 85 (manuscript received 24 Aug 83) pp 56-60

[Article by Ye. I. Il'ina-Kakuyeva and V. Ye. Novikov]

[English abstract from source] In the experiment rats were suspended in the head-down position (at  $-15$  to  $-20^\circ$ ) for 21 days. To study the effect of this exposure on skeletal muscles of their fore- and hindlimbs, morphological and histochemical methods were used. Changes in the hindlimbs were similar to those seen in real weightlessness of similar duration. The two antigravitational muscles--soleus and gastrocnemius muscles--showed greatest changes, i.e., atrophic and metabolic shifts. The biceps brachii muscle that changes insignificantly in the weightless state developed a destructive process (with degradation of myofibers) that was later replaced with a reparative process. The changes in this muscle are assumed to be associated with hemodynamic disorders. It is recognized that the method of rat suspension is adequate for a ground-based study of morphological effects of weightlessness on hindlimbs and is unacceptable for that of forelimbs where the exposure induces microcirculation disorders.

[Text] In recent years, various stands have been used to simulate some of the effects of weightlessness on rats, in which the animals are suspended in a head-down position, at an angle, by means of special devices [2, 9]. Such experimental models eliminate the load from the hind legs, rendering the functional state of the animals close to the one observed in weightlessness and causing redistribution of blood with its accumulation in the top of the trunk, as observed in cosmonauts on the first days of flight. Suspended rats can move freely in any direction and thus avoid hypokinesia.

We undertook this study to determine the effect of antiorthostatic position of rats, as produced by suspension, on muscles of the posterior and anterior extremities, i.e., muscles that are not only in a different functional state with the altered position of the trunk, but in different conditions of blood supply. The obtained data were evaluated from the standpoint of

adequacy of the model used to the morphological effects observed in muscles in weightlessness, and they were also compared to some of the changes that occur in muscles in the case of clinostatic hypokinesia.

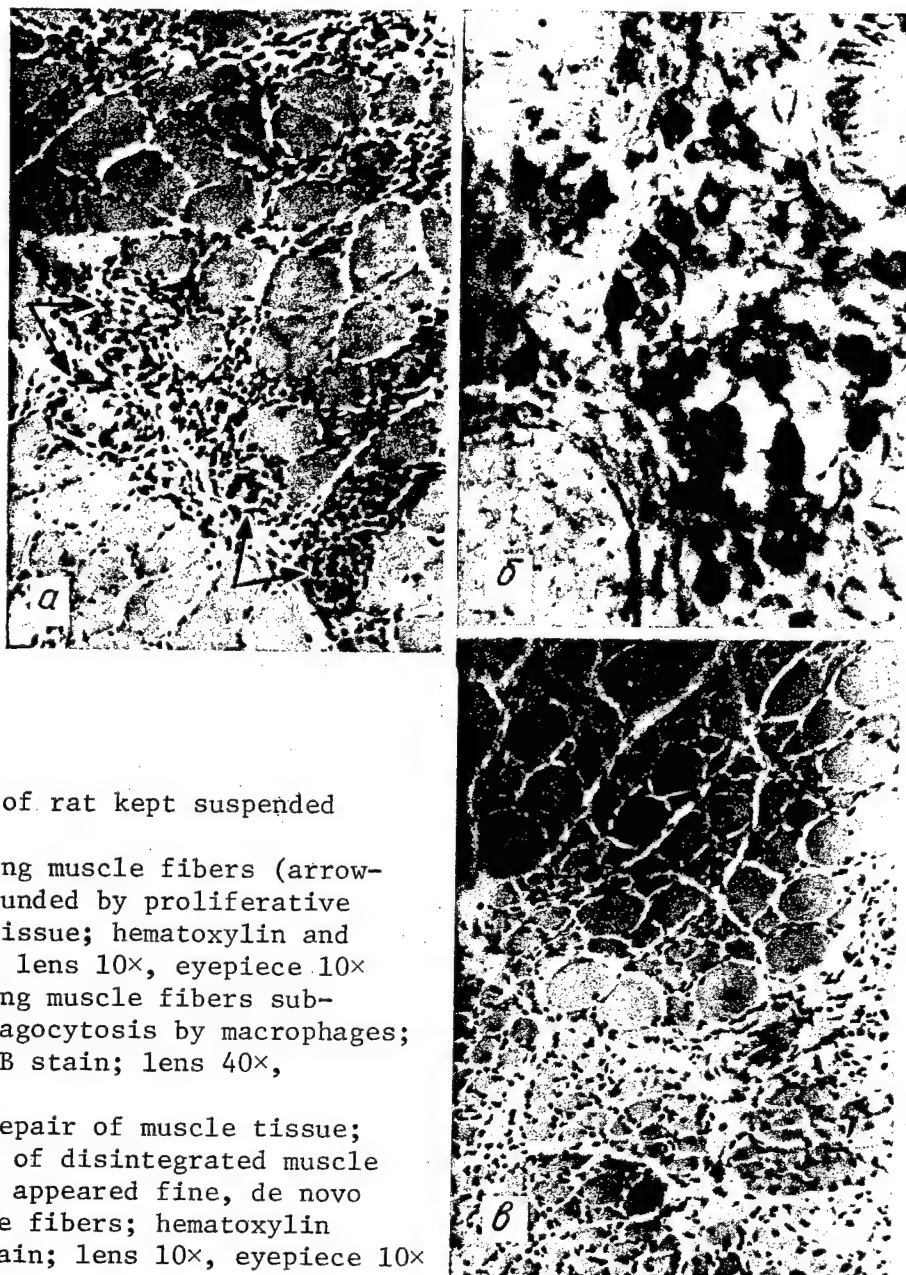
## Methods

We used 20 male Wistar rats in the experiment; they were 6 months old and average weight was 441 g. Ten animals were kept in antiorthostatic position, head down at an angle of  $-15-20^\circ$  for 21 days. In this position, the forelegs were subject to a greater load, whereas the hind legs were entirely without a load; however, motion was retained. The rats were secured in inclined position by the tail using adhesive tape, unlike the original model, in which a special capron [nylon] suit and wire frame were used to suspend the animal [2]. The animals could move in the cage on a special block and could take feed freely with their front legs. The other 10 rats served as a control. The animals were weighed before and after the experiment. They were sacrificed on the 21st day by intraperitoneal injection of thiopental in a dose of 50 mg/kg. We took the muscles of the hind legs for examination: soleus, gastrocnemius, anterior tibial, long digital extensor, femoral quadriceps, as well as one muscle from the forelegs, the brachial biceps. After being weighed, the muscles were frozen in freon-12 cooled with liquid nitrogen. In sections prepared in a cryostat, we assayed histochemically the activity of the following dehydrogenases:  $\text{NADH}_2$ , isocitrate (IsDH), malate (MDG),  $\alpha$ -ketoglutarate (KGIDH), glutamate (GIDH),  $\alpha$ -glycerophosphate bound and not bound with NAD (GPDHN, GPDH), succinate (SDH), activity of acid ATPase and ATPase of myosin [11]; we also demonstrated glycogen by the PAS method and phospholipids with sudan black B. In addition, the sections were stained with hematoxylin and eosin, as well as by the Mallory method. Enzyme activity was estimated visually, rating it on a 5-point scale. For morphometric studies, we used preparations, in which the types of muscle fibers were identified after demonstrating myosin ATPase activity in them. The preparations were photographed and negatives projected on paper, on which we traced 100 each red, white and intermediate muscle fibers. The outlined projections of fibers were cut out and weighed on an electronic balance. The numerical data from the gravimetric study, as well as parameters obtained from weighing the animal's muscles and carcass were submitted to statistical processing by the Student method.

## Results and Discussion

The obtained data indicate that there was no change in weight of experimental and control animals after the experiment, as compared to base values; however, the experimental animals had a tendency toward losing weight and controls, toward gain. On the last day of the experiment, experimental animals weighed 11.7% less than control rats ( $p < 0.002$ ).

Of the six muscles examined, only the soleus and gastrocnemius showed a reliable difference in weight. It was 14.7% and 13.7% less, respectively, than in control animals. According to the biometric data, only intermediate fibers were affected in the soleus; their cross section was 21.8% smaller than in the control ( $P < 0.01$ ) whereas in the gastrocnemius this applied to white fibers, which were 22.3% smaller than the control ( $P < 0.05$ ). Histochemically,



Brachial biceps of rat kept suspended for 21 days.

- a) disintegrating muscle fibers (arrowheads) surrounded by proliferative connective tissue; hematoxylin and eosin stain; lens 10×, eyepiece 10×
- b) disintegrating muscle fibers submitted to phagocytosis by macrophages; Sudan black B stain; lens 40×, eyepiece 10×
- c) section of repair of muscle tissue; in the place of disintegrated muscle fibers there appeared fine, de novo formed muscle fibers; hematoxylin and eosin stain; lens 10×, eyepiece 10×

metabolic changes were demonstrated in these two muscles. They consisted of significant increase in GPDH and, to a lesser extent, GPDHN activity, substantial decrease in SDH activity, some decline of G1DH, KG1DH activity and glycogen content, and increase in phospholipid content in the soleus. In the gastrocnemius, there was increase in GPDH activity, but to a lesser extent than in the soleus, and some decline in activity of MDH and G1DH; there was also increase in phospholipid content.

No morphological changes were demonstrated in muscles of the hind legs, with the exception of atrophic thinning of some muscle fibers in the

gastrocnemius and soleus. The brachial biceps was noteworthy because of changes indicative of destructive and repair processes which extended over most of its surface and were marked in all 10 experimental rats. Considerable portions of muscles with dying fibers, sealed in connective tissue and subject to phagocytosis by macrophages could be seen on preparations from some animals (see Figure, *a* and *o*). There was appreciable impairment of metabolism of such muscle fibers: disappearance of activity of oxidative enzymes, with the exception of GPDH, the activity of which increased significantly, and there was increase in lipid content. The destroyed fibers had no glycogen. In other animals, which made up the majority, there was prevalence of a repair process, manifested by appearance of thin, de novo formed muscle fibers that appeared in the place of dead muscle tissue (see Figure, *e*). Such sections of muscles presented abundant vascularization, numerous capillaries with high activity of acid ATPase in the endothelium invested each fiber compactly. The small regions of intact muscle tissue did not differ from the control in morphological or histochemical features. The marked polymorphism of muscle fibers, which appeared due to a pathological process, did not permit us to submit them to biometric analysis.

These studies revealed that, in rats kept suspended for 21 days, the changes in muscles of the posterior legs had much in common with those that develop in weightlessness of similar duration. This was also reported by Feller, Ginoza and Morrey, Musacchia, Steffen and Deavers [8, 10]. In both instances, the changes are manifested by muscular atrophy. Functionally, different muscles are not equally affected. The two main antigravity muscles, soleus and gastrocnemius, are primarily subject to this process. In addition, not all types of fibers are involved in each muscles, only one or two of them.

A very different process is observed in rats placed in box-cages to restrict movement. In this case, muscular atrophy does not develop; rather, there is drastic inhibition or arrest of growth as a whole and of muscles and muscle fibers in particular [5]. A comparison of muscle weight in these animals to that of control rats that continued to grow could create the false impression that they developed an atrophic process.

A comparison of the histochemical changes that occur in all muscles in anti-orthostatic position, clinostatic hypokinesia and weightlessness revealed one general fact: substantial change in activity of flavin oxidative enzymes in the soleus consisting of significant and sometimes excessive increase in GPDH activity and appreciable decline of SDH activity. At the same time, the activity of NAD-bound oxidative enzymes, if it did change, it was to a considerably lesser degree. It is quite probable that the cause of increase in GPDH activity is the need to utilize lipids released with mass-scale dissociation of membrane structures of muscle fibers undergoing atrophic and dystrophic processes. Evidently, the same can explain the increase in GPDH activity in the brachial muscle of suspended rats. The appreciable decrease in activity of SDH, which is one of the key enzymes in the Krebs cycle, insignificant change or absence of changes in activity of other enzymes of this cycle that were analyzed indicate that there is selective impairment in muscle fibers of the process of conversion of succinic acid, the cause of which is not clear at this time. In the gastrocnemius, the changes in oxidative enzyme activity were insignificant, and they were directly related to severity of muscular atrophy.

In spite of the similarity of some metabolic disturbances demonstrated histochemically in muscles of suspended rats under clinostatic hypokinetic conditions and in weightlessness, there are also differences between parameters obtained in weightlessness and ground-based experiments. They are referable to excessive accumulation of glycogen in all skeletal muscles in the case of weightlessness due to elimination of static load on muscles, since this effect did not occur in a biosatellite with artificial gravity [3]. Conversely, a decrease in muscle glycogen content is observed in rats in antiorthostatic position and submitted to clinostatic hypokinesia [1, 6, 7].

As noted above, the model with suspension of rats has the purpose not only of relieving the load on hindlimb muscles, but eliciting redistribution of blood in the body with its accumulation in the head end of the trunk, i.e., obtaining one of the effects observed in weightlessness. It was found that the vascular system of foreleg muscles is not indifferent to such a position of the body. This is indicated by the destructive and repair processes in the brachial biceps. We previously observed appearance of analogous changes in the soleus of rats kept in small hypokinetic cages, as well as after exposure to weightlessness [4]. Investigation of the dynamics of the process led us to conclude that it is based on circulatory disturbance arising for some reason or other. No doubt, the pathological process in the brachial biceps is also based on a hemodynamic disturbance. We can conceive of the mechanism leading to death of muscle tissue as follows: venous stasis develops in the muscle due to redistribution of blood in the body, increased load on the forelegs and inadequate efficiency of the muscle pump; this leads to edema of the muscle which, in turn, impairs trophics of muscle fibers and elicits tissular hypoxia. The last two factors are the immediate cause of destruction of fibers. Judging from the fact that there was prevalence on the 21st experimental day of a repair process in the muscle, as a result of which many young muscle fibers appeared and, at the same time, there was a process of active resorption of already destroyed muscle fibers that had undergone phagocytosis by macrophages, it can be assumed that the acute manifestations of circulatory disturbances occurred at the earlier stages, probably on the first days after suspending the rats. Subsequently, the vascular system adapted to new functioning conditions. Numerous new capillaries appeared, which proliferated into connective tissue, and recovery of muscle tissue proper began.

Thus, this investigation convinced us that the model with suspension of rats is the most adequate one for ground-based studies of effects that arise in skeletal muscles, mainly of the posterior extremities, in weightlessness. We also obtained data to the effect that redistribution of blood and its accumulation in the head end of the trunk could cause serious circulatory disturbances in muscles of the front legs, which lead to destruction of muscle tissue and have an adverse effect on their function.

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EFFECT OF BRIEF HEAT ON TISSULAR RESPIRATION OF SKELETAL MUSCLES AND  
VISCERA OF HYPOKINETIC CHICKENS

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[Article by M. S. Talipov and O. N. Bogoyavlenskaya]

[English abstract from source] The effect of high temperature (35°C) on the gas exchange and tissue respiration of skeletal muscles and viscera of 47 chickens weighing 1100-1700 g was investigated on hypokinesia days 1, 20, 40 and 60. After 2 hour thermal exposure the rate of oxidate processes decreased, particularly on day 40. Oxygen consumption by femur, chest, neck and heart muscles decreased and that by back muscles did not change on hypokinesia days 30 and 60. Carbon dioxide production by various muscles was lower on day 20 and unchanged on day 60. The respiration quotient of the skeletal muscles and viscera increased on hypokinesia days 1 and 60. It can therefore be concluded that thermal exposure combined with hypokinesia produces not only quantitative but also qualitative metabolic changes.

[Text] As we know, the muscular system, which constitutes an average of up to 40% of body mass, holds an important place in systemic thermogenesis. A functional decline of the muscular system has an adverse effect on the body's adaptive mechanisms, functions of different organs and systems [1, 5-7, 12, 15-18]. Under such conditions, there is impaired assimilation of carbohydrates by muscle tissue, and the role of lipids increases as sources of energy [9, 16].

All these changes affect dynamic and static efficiency of the body [5]. However, the question of involvement of different groups of skeletal muscles and internal organs in thermogenesis with exposure to various extreme factors, namely with restricted motor activity of animals exposed to high ambient temperature, remains unexplored.

We investigated here the effect of short-term heat loads on tissue respiration of various groups of skeletal muscles and organs (liver and heart) of chicken submitted to long-term hypokinesia.

## Methods

Experiments were conducted in the fall on 47 chickens weighing 1100-1700 g. The experimental group (38) was submitted to hypokinesia (2 chickens per cage 45×90×45 cm in size) for 60 days at room temperature (20-22°C). Control fowl were kept in the same room without restriction of movement. At the end of the 1st, 20th, 40th and 60th days of immobility, some of the experimental and control chickens were exposed to a temperature of 35°C in an incubator at 26-40% relative air humidity for 2 h, after which they were decapitated and organs taken for analysis.

Oxygen uptake and carbon dioxide output were analyzed in muscle (cervical, femoral, thoracic and dorsal) paste, liver and heart tissue using Warburg apparatus at bath temperature of 37°C [13, 14]. The incubation medium consisted of potassium phosphate buffer (40  $\mu$ M, pH 7.4), magnesium chloride (10  $\mu$ M) and potassium chloride (200  $\mu$ M) without addition of oxidation substrate. We recorded muscle mass of viscera and body temperature. The obtained results were submitted to statistical processing by the method of small samples [11].

## Results and Discussion

The results of studies conducted at high ambient temperature revealed that there is appreciable change in intensity of metabolism in both control and experimental chickens. The Figure shows that, with 2-h exposure to heat, respiration of femoral, cervical and thoracic muscles of control fowl had a tendency toward decline, but the changes were reliable only in the femoral muscle. Oxygen uptake and carbon dioxide output by this tissue were 35.1 and 36.3% lower, respectively, than base values. Under these conditions there was intensification of respiratory activity of dorsal muscles. These changes were reflected in overall respiration of skeletal muscles, and muscular oxygen uptake per 100 g body weight was 12.1% lower (see Table).

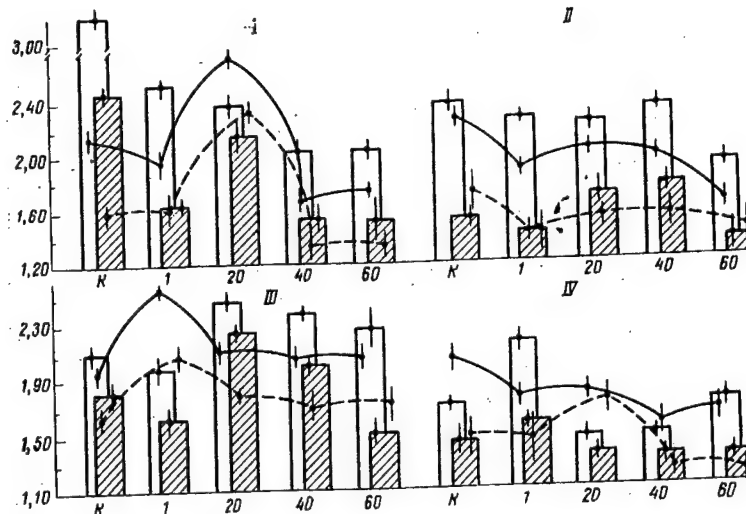
Under these conditions we failed to demonstrate noticeable changes in intensity of metabolism of hepatic tissue. Metabolic activity of the myocardium was drastically depressed under the effect of the heat factor: overall oxygen uptake (per 100 g body weight) was 15.3% lower and carbon dioxide output 21.9% higher. The demonstrated changes in gas exchange of muscles of the thigh, neck, chest and cardiac tissue had some influence on overall level of oxidative processes, namely, with 2-h exposure to a heat load oxygen uptake by fowl kept on the usual regimen of movement dropped by 13.2% (from  $797 \pm 29$  to  $629 \pm 35$   $\mu$ l per kg body weight per hour).

Identical changes were noted in overall gas exchange in fowl under hypokinetic conditions with exposure to heat. Two-hour exposure at the early stage of hypokinesia (1st and 20th days) had no effect on gas exchange, although oxygen uptake on the whole had a tendency toward declining. Thus, while oxygen uptake (on 1st and 20th days of restricted movement) constituted  $756 \pm 31$  and  $639 \pm 47$  ml/kg/h at room temperature, after 2-h heat exposure it did not exceed  $697 \pm 33$  and  $571 \pm 56$  ml/kg/h. This difference grew even more by the 40th day: oxygen uptake decreased by 15.1% with overheating.

Total oxygen uptake ( $QO_2$ ), carbon dioxide output ( $QCO_2$ ) and respiratory quotient in tissues of experimental and control chickens at different ambient temperatures

| Hypokinesia,<br>days | Metabolism, $\mu\text{l}/100 \text{ g/l h}$ |                    |                        | Tissue weight,<br>$\text{g}/100 \text{ g body weight}$ |
|----------------------|---|--------------------|------------------------|--|
|                      | $QO_2$                                      | $QCO_2$            | Respiratory quotient   |  |
| In muscles           |   |                    |                        |  |
| Control              | $14\ 774 \pm 703$                           | $11\ 276 \pm 843$  | $0.76 \pm 0.09$ (32)   | $53.8 \pm 1.1$   |
|                      | $13\ 098 \pm 363^*$                         | $10\ 327 \pm 186$  | $0.79 \pm 0.04$ (31)   | $53.0 \pm 1.3$   |
| 1                    | $14\ 144 \pm 521$                           | $10\ 160 \pm 467$  | $0.72 \pm 0.03$ (29)   | $52.8 \pm 0.8$   |
|                      | $13\ 757 \pm 650$                           | $11\ 113 \pm 786$  | $0.81 \pm 0.03^* (27)$ | $54.0 \pm 0.9$   |
| 20                   | $13\ 029 \pm 479$                           | $11\ 026 \pm 678$  | $0.85 \pm 0.02$ (31)   | $51.6 \pm 1.5$   |
|                      | $13\ 244 \pm 497$                           | $11\ 390 \pm 236$  | $0.86 \pm 0.08$ (32)   | $54.0 \pm 0.5$   |
| 40                   | $13\ 005 \pm 497$                           | $10\ 257 \pm 550$  | $0.79 \pm 0.04$ (30)   | $51.9 \pm 0.3$   |
|                      | $10\ 713 \pm 423^*$                         | $8\ 532 \pm 470^*$ | $0.79 \pm 0.02$ (29)   | $49.5 \pm 1.5$   |
| 60                   | $11\ 938 \pm 715$                           | $8\ 775 \pm 425$   | $0.73 \pm 0.03$ (27)   | $49.7 \pm 0.5$   |
|                      | $10\ 407 \pm 278^*$                         | $9\ 025 \pm 464$   | $0.87 \pm 0.02^* (31)$ | $51.2 \pm 0.8$   |
| In liver             |   |                    |                        |  |
| Control              | $586 \pm 84$                                | $362 \pm 54$       | $0.62 \pm 0.07$ (7)    | $0.22 \pm 0.04$  |
|                      | $555 \pm 54$                                | $364 \pm 39$       | $0.66 \pm 0.04$ (7)    | $0.22 \pm 0.02$  |
| 1                    | $553 \pm 62$                                | $376 \pm 32$       | $0.68 \pm 0.03$ (7)    | $0.22 \pm 0.02$  |
|                      | $531 \pm 67$                                | $317 \pm 42$       | $0.59 \pm 0.04$ (8)    | $0.21 \pm 0.02$  |
| 20                   | $540 \pm 23$                                | $375 \pm 36$       | $0.69 \pm 0.06$ (9)    | $0.23 \pm 0.02$  |
|                      | $552 \pm 44$                                | $350 \pm 56$       | $0.63 \pm 0.09$ (9)    | $0.22 \pm 0.01$  |
| 40                   | $536 \pm 36$                                | $339 \pm 37$       | $0.63 \pm 0.04$ (8)    | $0.22 \pm 0.02$  |
|                      | $704 \pm 45^*$                              | $359 \pm 29$       | $0.51 \pm 0.02^* (9)$  | $0.22 \pm 0.02$  |
| 60                   | $683 \pm 53$                                | $416 \pm 81$       | $0.61 \pm 0.07$ (6)    | $0.23 \pm 0.02$  |
|                      | $632 \pm 61$                                | $464 \pm 41$       | $0.73 \pm 0.04$ (7)    | $0.23 \pm 0.03$  |
| In heart             |   |                    |                        |  |
| Control              | $118 \pm 6$                                 | $86 \pm 10$        | $0.72 \pm 0.08$ (6)    | $0.45 \pm 0.05$  |
|                      | $108 \pm 5$                                 | $94 \pm 7$         | $0.94 \pm 0.004^* (6)$ | $0.48 \pm 0.05$  |
| 1                    | $79 \pm 6$                                  | $55 \pm 5$         | $0.70 \pm 0.04$ (7)    | $0.39 \pm 0.03$  |
|                      | $81 \pm 15$                                 | $66 \pm 6$         | $0.81 \pm 0.03^* (5)$  | $0.45 \pm 0.07$  |
| 20                   | $94 \pm 5$                                  | $76 \pm 8$         | $0.81 \pm 0.06$ (6)    | $0.41 \pm 0.04$  |
|                      | $112 \pm 7$                                 | $98 \pm 10$        | $0.88 \pm 0.08$ (6)    | $0.49 \pm 0.03$  |
| 40                   | $107 \pm 16$                                | $80 \pm 12$        | $0.75 \pm 0.08$ (6)    | $0.55 \pm 0.07$  |
|                      | $96 \pm 6$                                  | $80 \pm 7$         | $0.83 \pm 0.06$ (8)    | $0.49 \pm 0.05$  |
| 60                   | $129 \pm 10$                                | $76 \pm 7$         | $0.59 \pm 0.08$ (5)    | $0.48 \pm 0.02$  |
|                      | $104 \pm 4^*$                               | $102 \pm 7^*$      | $0.98 \pm 0.04^* (7)$  | $0.55 \pm 0.02^*$                                      |

Note: Numerator gives data at room temperature (20-22°C) and denominator, with exposure to high temperature (35°C; number of measurements given in parentheses). Asterisk indicates reliable differences in relation to level at room temperature ( $P < 0.05$ ).



Dynamics of oxygen uptake and carbon dioxide output by skeletal muscles of control and experimental chickens at room temperature and with exposure to high temperature

X-axis, day of examination; y-axis, oxygen uptake and carbon dioxide output ( $\mu\text{l}/\text{mg dry weight/h}$ ). I-IV--femoral, cervical, thoracic and dorsal muscles, respectively. White bars--oxygen uptake; striped--carbon dioxide output at room temperature; solid and dash lines--oxygen uptake and carbon dioxide output at high temperature.

Diminished thermogenesis at high ambient temperature is effected by depression of respiratory activity of both individual organs and different groups of skeletal muscles. However, the degree of their involvement in the body's response to heat is not the same, and it depends to some extent on the functional purpose of the muscle and duration of hypokinesia (see Figure). Thus, 2-h exposure on the 1st day of hypokinesia depresses intensity of oxidative processes by 18.7-22.6% in the dorsal, cervical and femoral muscles and enhances them by 29.7% in the thoracic muscle. Under these conditions, the amount of carbon dioxide discharged by tissues of all muscle groups (with the exception of thoracic) underwent virtually no change, while the respiratory quotient rose drastically in muscles of the thigh (from  $0.66 \pm 0.05$  to  $0.83 \pm 0.05$ ), neck (from  $0.63 \pm 0.05$  to  $0.76 \pm 0.02$ ) and back (from  $0.74 \pm 0.05$  to  $0.84 \pm 0.06$ ).

The reaction of skeletal muscles was different on the 20th day of hypokinesia: respiration of thoracic muscle was less intensive, whereas that of the femoral and dorsal ones was more intense (see Figure).

Under these conditions, intensity of visceral (liver and heart) metabolism on the 1st and 20th day of restricted movement remained unchanged; myocardial respiration increased somewhat by the end of the 20th experimental day (see Table). With 2-h exposure to heat, the rate of oxygen uptake by skeletal muscles and the myocardium was noticeably inhibited at the end of the 40th and 60th days of hypokinesia. As a result, overall oxygen uptake by skeletal muscles and cardiac tissue diminished (see Table). During these

periods, there was no appreciable change in tissular output of carbon dioxide, while the respiratory quotient of both internal organs and skeletal muscles rose noticeably on the 60th experimental day.

With 2-h heat exposure, there was no appreciable change in relative mass of internal organs and skeletal muscles of fowl; only myocardial mass was somewhat altered (see Table). These changes occurred against the background of elevated rectal temperature, which rose in both control and experimental fowl when exposed to heat. However, there was a greater increment in control chickens than experimental ones. Thus, while rectal temperature rose by  $2.5^{\circ}\text{C}$  (from  $39.70 \pm 0.03$  to  $42.2 \pm 0.03$ ) with 2-h heat exposure after 1-day intoxication [sic], at the end of the 40th and 60th days of hypokinesia it rose by only  $1.4$  and  $1.1^{\circ}\text{C}$  (from  $40.4 \pm 0.04$  to  $41.8 \pm 0.02$  and from  $41.1 \pm 0.4$  to  $42.2 \pm 0.6$ ), which is confirmed by the data of P. V. Vasil'yev et al. [4] who investigated the effect of high temperature ( $40-42^{\circ}\text{C}$ ) on heat-regulating function in white rats after 15- and 30-day hypokinesia: rectal temperature increment was less marked in experimental animals than controls. When exposed to various environmental stressors (hypokinesia combined with high temperature), the body retains its temperature homeostasis by reducing heat production in tissues of different organs. For this reason, oxygen uptake diminishes in skeletal muscles and some organs (heart). The decline in intensity of oxidative processes in control chickens exposed to high temperature occurs mainly due to respiration of femoral and cardiac muscles, whereas in experimental fowl (on 40th and 60th days of hypokinesia) this is maintained by all muscles groups and heart tissue. Under these conditions, the respiratory quotient rises in chicken skeletal muscles and myocardium. Consequently, not only quantitative, but qualitative changes in metabolic processes occur in the body, as confirmed by data in the literature.

T. V. Kosolapova [8] and A. M. Nasyrova [10] reported a decrease in reserve of glycogen and total lipids of muscles and some internal organs of chickens submitted to hypokinesia combined with high ambient temperature.

It is known that elevation of lactic acid levels in different organs and pyruvic acid content of blood under the effect of high temperature elicits considerable expenditure of glycogen which causes prevalence of anaerobic route and acceleration of glycolysis, as a result of which there is slower delivery of oxygen to tissues [2, 3, 10].

As indicated by the above data, stressors (hypokinesia and high ambient temperature) have a significant effect on the body, as manifested by change in body temperature, overall level of metabolism, as well as tissular metabolism in different organs and systems.

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#### EFFECT OF ACUTE HYPOXIA ON CORONARY AND SYSTEMIC HEMODYNAMICS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 15 Apr 83) pp 64-68

[Article by V. S. Bednenko, V. N. Polyakov, M. V. Dvornikov, V. K. Stepanov and A. N. Kozlov]

[English abstract from source] Variations in coronary circulation, cardiac output and heart rate were examined by dopplerography in 14 test subjects kept in an altitude chamber. It was found that during acute hypoxia the effective coronary blood flow decreased distinctly prior to general circulatory disorders. It is recommended to monitor coronary circulation during altitude exposures.

[Text] In some emergency situations in flight, acute hypoxic hypoxia could become the prime extreme factor and determine the limit of pilot efficiency at high altitude. In spite of the fact that there are many works dealing with the problem of hypoxia under such conditions [6, 7, 9, 10], questions of intensity of function of mechanisms regulating coronary circulation, which largely determine hypoxia endurance time, have still not been sufficiently explored. The objective of our work was to assess the functional distinctions of these mechanisms.

#### Methods

We conducted 14 studies of 11 healthy subjects 19-20 years of age in a pressure chamber with rarefaction to 321 mm Hg and breathing air. Exposure time at "high altitudes" was governed by time of onset of drastic worsening of wellbeing and general condition (according to observation of subjects' behavior and parameters of physiological functions).

We recorded the ECG in the D-S lead, blood pressure (BP) in the brachial artery by the Korotkov method and ultrasonic dopplerography (UDCG) from a region that enabled us to locate the posterior wall of the left ventricle of the heart (6th left intercostal space near the sternum) [1]. We determined heart rate (HR), systolic and diastolic blood pressure. We calculated dynamic mean pressure using the formula of Hickam. We assessed the dynamics of stroke effective coronary blood flow (ECF) from the integral

values of UDCG signal level in systole; ECF reflects the amount of blood flowing through coronary vessels and giving off oxygen to myocardial capillaries [1, 2]. From the integral values of UDCG frequency in the ejection period, we determined the dynamics of stroke output (SO) by the heart scaled to increment in volume of the left ventricle [1, 3].

Relative changes in ECF ( $Q_{rel}$ ) and stroke output ( $SO_{rel}$ ) were calculated using the formulas,  $Q_{rel} = A_h/A_b$  and  $ECF_{rel} = F_h/F_b$ , where  $A_h$  and  $F_h$  are integral values of signal level in systole and signal frequency in ejection period, respectively, under the effect of hypoxia;  $A_b$  and  $F_b$  are the same in the base state (background). We calculated the relative changes in minute ECF ( $MECF_{rel}$ ) and circulation volume  $CV_{rel}$  using the following formulas:  $MECF_{rel} = Q_{rel} \cdot HR_{rel}$  and  $CV_{rel} = SV_{rel} \cdot HR_{rel}$ , where  $HR_{rel} = HR_h/HR_b$ , ratio of HR with exposure to hypoxia ( $HR_h$ ) to base HR ( $HR_b$ ). We calculated the general parameter of dynamics of amplitude and frequency components of UDCG, which characterize the relative changes in energy of cardiac contractions  $W_{rel}$  [8] using the formula,  $W_{rel} = [(A_{cc})_h \cdot (F_{cc})_h] / [(A_{cc})_b \cdot (F_{cc})_b]$ , where  $(A_{cc})_h$  and  $(F_{cc})_h$  are integral values of signal level and frequency during cardiac cycle with hypoxia,  $(A_{cc})_b$  and  $(F_{cc})_b$  are the same values in the base state. The integral values of parameters were found using digital converters [1]. External respiration function was assessed by conventional methods [9] from the values of its frequency and pulmonary ventilation (minute respiratory volume), as well as partial oxygen and carbon dioxide tension ( $p_{A_{O_2}}$  and  $p_{A_{CO_2}}$ ) in alveolar air.

## Results and Discussion

The subjects spent an average of  $17.0 \pm 1.4$  min at "high altitude, while time of exposure to hypoxia corresponding to appearance of early signs of worsening of their condition (hyperkinetic disorders, early forms of tremor, etc.) was  $10.3 \pm 1.1$  min.

The dynamics of external respiration functions corresponded to development of moderate hyperventilation (1.5-fold or greater increase in frequency and minute respiratory volume) and hypocapnia (decline of partial carbon dioxide tension to 20 mm Hg) (Table 1).

[Beginning of first paragraph on source p 66 is missing]

...these parameters occurred in the 3d min, after which there was relative stabilization. This was associated with  $p_{A_{O_2}}$  of 35-37 mm Hg.

On the whole, hemodynamic reactions were characterized by changes aimed at intensifying circulatory function: all recorded hemodynamic parameters usually underwent reliable changes starting in the 3d-5th min of exposure.

On the average, HR increased appreciably by the 3d-7th min of hypoxia, from 66 to 89-98/min, after which this parameter became stabilized. Upon appearance of early signs of worsening of the subjects' condition, there was an even greater rise of HR, to 112/min. The recorded values virtually coincided with results obtained in several studies during flight in aircraft and ascents in a pressure chamber [10].

Table 1. Parameters of hemodynamics and external respiration with exposure to hypoxia (Mim)

| Parameter                              | Base state | Exposure time, min* |                    |                    |                    |                    |                 |                    |                    |                 | With ear<br>ly signs<br>of decompensation | Before<br>"descent" |
|--|------------|---------------------|--------------------|--------------------|--------------------|--------------------|-----------------|--------------------|--------------------|-----------------|---|---------------------|
|  |            | 1                   | 3                  | 5                  | 7                  | 10                 | 12              | 15                 | 17                 | 20              |   |                     |
| HR/min                                 | 66±3       | 61±4<br>>0,05       | 89±4<br><0,001     | 92±4<br><0,001     | 98±4<br><0,001     | 96±4<br><0,001     | 98±6<br><0,001  | 99±4<br><0,001     | 93±5<br><0,001     | 88±10<br><0,05  | 112±3<br><0,001                           | 94±6<br><0,001      |
| BP, mm Hg:                             | P          |                     |                    |                    |                    |                    |                 |                    |                    |                 |   |                     |
|  |            |                     |                    |                    |                    |                    |                 |                    |                    |                 |   |                     |
| systolic                               | 129±2      | 136±2<br><0,05      | 134±3<br>>0,05     | 135±3<br>>0,05     | 142±2<br><0,001    | 138±3<br><0,02     | 145±2<br><0,001 | 152±3<br><0,001    | 154±3<br><0,001    | 149±3<br><0,001 | 148±4<br><0,001                           | 148±3<br><0,001     |
| diastolic                              | 61±2       | 65±2<br>>0,05       | 59±2<br>>0,05      | 57±3<br>>0,05      | 54±2<br><0,05      | 54±2<br><0,05      | 54±2<br><0,01   | 54±3<br>>0,05      | 54±2<br><0,05      | 56±4<br>>0,05   | 48±1<br><0,001                            | 53±2<br><0,001      |
| mean dynamic                           | 84±3       | 88±3<br>>0,05       | 84±3<br>>0,05      | 83±4<br>>0,05      | 81±3<br>>0,05      | 82±3<br>>0,05      | 84±3<br>>0,05   | 87±3<br>>0,05      | 87±3<br>>0,05      | 87±5<br>>0,05   | 81±4<br>>0,05                             | 85±3<br>>0,05       |
| Respiration rate/<br>min               | 13±1       | 15±1<br>>0,05       | 16±1<br><0,05      | 14±1<br>>0,05      | 16±1<br><0,05      | 16±1<br><0,05      | —               | 18±1<br><0,01      | 18±1<br><0,01      | —               | —   | 18±1<br><0,01       |
| Minute respiratory<br>volume, l/min    | 9,3±0,2    | 11,6±0,9<br><0,02   | 15,3±0,9<br><0,001 | 14,1±0,8<br><0,001 | 15,2±0,8<br><0,001 | 15,2±0,6<br><0,001 | —               | 15,4±0,9<br><0,001 | 15,7±1,6<br><0,001 | —               | —   | 15,7±1,6<br><0,001  |
| P <sub>A</sub> O <sub>2</sub> , mm Hg  | 108±1      | 39±1<br><0,001      | 36±1<br><0,001     | 35±1<br><0,001     | 36±1<br><0,001     | 37±1<br><0,001     | —               | 37±1<br><0,001     | 37±1<br><0,001     | —               | —   | 37±1<br><0,001      |
| P <sub>A</sub> CO <sub>2</sub> , mm Hg | 36±0,4     | 22±0,5<br><0,001    | 22±0,4<br><0,001   | 22±0,6<br><0,001   | 21±0,6<br><0,001   | 21±0,6<br><0,001   | —               | 20±0,6<br><0,001   | 20±0,9<br><0,001   | —               | —   | 20±0,9<br><0,001    |

\*Data for 20th min of exposure are characterized by decline to 5 in volume of statistical sample.

Table 2. Dynamics of parameters of coronary circulation and myocardial contractile function with exposure to hypoxia (M±m)

| Relative change in parameter | Exposure time, min      |                          |                          |                          |                          |                          |                          |                         | With early signs of decompen. | Before "descent"         |
|------------------------------|-------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-------------------------|-------------------------------|--------------------------|
|                              | 1                       | 3                        | 5                        | 7                        | 10                       | 12                       | 15                       | 17                      | 20                            |                          |
| Stroke ECF                   | 1.24 ± 0.10<br>P < 0.05 | 1.63 ± 0.20<br>P < 0.01  | 1.46 ± 0.12<br>P < 0.001 | 1.70 ± 0.18<br>P < 0.001 | 1.91 ± 0.23<br>P < 0.001 | 2.11 ± 0.31<br>P < 0.01  | 2.13 ± 0.29<br>P < 0.001 | 1.46 ± 0.18<br>P < 0.02 | 1.31 ± 0.15<br>P < 0.05       | 2.05 ± 0.53<br>P < 0.05  |
| Minute ECF                   | 1.30 ± 0.18<br>P > 0.05 | 2.18 ± 0.37<br>P < 0.01  | 2.14 ± 0.23<br>P < 0.001 | 2.55 ± 0.36<br>P < 0.001 | 3.01 ± 0.41<br>P < 0.001 | 3.26 ± 0.56<br>P < 0.001 | 3.24 ± 0.55<br>P < 0.001 | 2.47 ± 0.43<br>P < 0.01 | 1.81 ± 0.20<br>P < 0.001      | 3.35 ± 0.98<br>P < 0.05  |
| SO                           | 1.09 ± 0.06<br>P > 0.05 | 1.23 ± 0.13<br>P > 0.05  | 1.36 ± 0.10<br>P < 0.01  | 1.52 ± 0.11<br>P < 0.001 | 1.57 ± 0.15<br>P < 0.001 | 1.79 ± 0.15<br>P < 0.001 | 1.59 ± 0.13<br>P < 0.001 | 1.63 ± 0.20<br>P < 0.01 | 1.58 ± 0.22<br>P < 0.02       | 1.51 ± 0.17<br>P < 0.01  |
| Min.resp. volume             | 1.18 ± 0.10<br>P > 0.05 | 1.75 ± 0.22<br>P < 0.01  | 1.86 ± 0.20<br>P < 0.001 | 2.35 ± 0.22<br>P < 0.001 | 2.47 ± 0.28<br>P < 0.001 | 2.68 ± 0.31<br>P < 0.001 | 2.58 ± 0.24<br>P < 0.001 | 3.08 ± 0.60<br>P < 0.01 | 2.08 ± 0.28<br>P < 0.001      | 2.31 ± 0.30<br>P < 0.001 |
| W                            | 1.34 ± 0.20<br>P > 0.05 | 2.49 ± 0.32<br>P < 0.001 | 2.33 ± 0.31<br>P < 0.001 | 3.46 ± 0.45<br>P < 0.001 | 3.75 ± 0.46<br>P < 0.001 | 3.57 ± 0.46<br>P < 0.001 | 4.25 ± 0.45<br>P < 0.001 | 4.21 ± 0.92<br>P < 0.01 | 2.88 ± 0.66<br>P < 0.02       | 4.06 ± 0.72<br>P < 0.001 |
|                              |                         |                          |                          |                          |                          |                          |                          |                         |                               | 1.87 ± 0.23<br>P < 0.001 |
|                              |                         |                          |                          |                          |                          |                          |                          |                         |                               | 3.02 ± 0.46<br>P < 0.001 |
|                              |                         |                          |                          |                          |                          |                          |                          |                         |                               | 1.61 ± 0.14<br>P < 0.001 |
|                              |                         |                          |                          |                          |                          |                          |                          |                         |                               | 2.50 ± 0.21<br>P < 0.001 |
|                              |                         |                          |                          |                          |                          |                          |                          |                         |                               | 4.25 ± 0.43<br>P < 0.001 |

Note: All parameters normalized to base values and expressed in relative units.

Up to the 17th min at "high altitude" we observed rise of systolic (increment up to 25 mm Hg), decline of diastolic (to 7 mm Hg) and slight (3-4 mm Hg) changes in mean dynamic BP. With development of early signs of decompensation the diastolic pressure drop reached 13 mm Hg and mean dynamic, 3 mm Hg.

Table 2 lists ratios of experimental parameters calculated from UDCG to their base values.

Stroke ECF increased under the effect of hypoxia by 1.63 times by the 3d min and more than 2 times by the 15th min. Starting in the 17th min, stroke ECF dropped distinctly, but still remained above the base value (1.43 in relation to background). Before descent ECF was lower than with development of early signs of decompensation.

Minute ECF increased by more than 2 times by the 3d min and about 3 times by the 15th min. Thereafter, like stroke coronary blood flow, it underwent a marked decline. The dynamics of minute and stroke ECF before descending from "high altitude" and with development of early signs of deterioration of condition were similar.

The results are consistent with the findings of many authors, who reported distinct intensification of coronary blood flow under the effect of hypoxia, due to marked dilatation of coronary vessels [6, 9, 10]. Since oxygenation of arterial blood drops to 50-75% of base values with the extent of rarefaction used [10], ECF is maintained at the above-indicated level due to 2.5-3-fold increase in total stroke coronary blood flow and 3.8-4.5-fold increase in minute coronary blood flow. These values are close to the physiological range of changes in blood supply to the myocardium in healthy people [11, 13], and they indicate that virtually all of the physiological reserve for increasing delivery of blood is depleted under these conditions.

There was a significant increase in stroke blood volume from the 5th to 20th min of exposure in 12 out of 14 cases; maximum values constituted 1.57-1.79 in relation to base levels. Circulation volume increased by 2-3 times, reaching a maximum by the 17th min. Before descent from "high altitude," both these parameters were higher than with development of early signs of decompensation. On the average by the 3d min, circulation volume was formed more at the expense of heart rate than stroke output; in the 5th-7th min, their relative contribution evened out, and from the 7th to 20th min the contribution of stroke output was 1.21-1.31 times greater. We should mention that there were some differences in individual mechanisms of formation of circulation volume. In 12 cases, its increase occurred against the background of increase in stroke output and in 2 cases, with decrease of the latter (to 0.69-0.91). This is consistent with the results obtained in [4].

In analyzing our results as a whole, it should be noted that with progression of hypoxia the changes in most hemodynamic parameters first reached a maximum (by 15th-17th min of exposure) then had a tendency toward declining. Evidently, progressive accentuation of hemodynamic reactions reflex a period of brief emergency adaptation to hypoxia, which continues until there is complete depletion of physiological reserves, onset of critical reactions and disruption of adaptation. It is important to stress that, prior to disruption of adaptation, the parameters of pumping (biomechanical) function of the myocardium (stroke output, minute volume of circulation, energy of cardiac contractions) were still on a high level and even presented some tendency toward further rise. However, at this time, stroke and minute ECF already started to decline distinctly (synchronously with decline of HR), which led to drastic intensification of processes of accumulation of incompletely oxidized metabolic products in cardiac tissues. It can be assumed that anaerobic metabolic processes play some part in holding the parameters of pumping function of the myocardium on a high level. However, this route of replacement of macroergic phosphates in cardiac tissues is 1/19th as efficient as the aerobic route [5], and glycogen content would be depleted within a few minutes [12]. In addition, accumulation of lactic acid formed with anaerobic glycolysis [14] would no doubt worsen even more the inconsistency between blood supply to the myocardium and its metabolic requirements.

Thus, in the overall pattern of circulatory disorders under the effect of acute hypoxic hypoxia, the decline of ECF precedes somewhat the changes in stroke output, minute circulation volume and energy of cardiac contractions. The presence of dynamics in different directions under these conditions, along with decrease of HR used to determine the time of worsening of condition [9, 10] is the sign of development of critical reactions. Since coronary circulation is characterized by a high level of metabolism, even at rest [5, 11], impairment of the correlation between metabolic requirements of the myocardium and coronary blood flow would lead to marked aggravation of myocardial hypoxia and could be a sign of development of acute coronary insufficiency. In view of the fact that tests in altitude chambers are used routinely in expert medical certification of flight personnel, while problems of stress versus normal with regard to reactions of coronary circulatory reactions under these conditions have not yet been fully resolved [10], one should consider it promising to use the method of monitoring ECF according to the UDCG to assess tolerance to hypoxia and detect latent forms of coronary insufficiency.

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## EFFECT OF DIBAZOL ON PARAMETERS OF NONSPECIFIC RESISTANCE OF SUBJECTS IN PRESSURIZED CABINS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 12 Mar 84) pp 68-71

[Article by V. S. Novikov and V. N. Bortnovskiy]

[English abstract from source] Prophylactic administration of dibazol (5 mg/day) prevents a decrease of nonspecific resistance and ensures stable variations of adaptation processes in men working in enclosures for a long time. The positive effect of the drug occurs 10-15 days after the administration and involves a combined action on phagocytosis, blood homeostasis, and skin antimicrobial resistance. The integrated parameters of nonspecific protection of the test subjects who took dibazol are close or even better than the pretest level. For instance, the efficiency of intracellular digestion increases and the microbial content of blood decreases. Coincidentally, the health condition improves and physical work capacity increases. Dibazol also exerts a beneficial effect on the adaptive process and morbidity rate of the subjects. The data obtained suggest that dibazol affects favorably the nonspecific resistance of the human body. In view of this, it can be recommended as a stimulating and training agent.

[Text] It is known that dibazol is among the agents that have an adaptogenic action [7]. This drug is used extensively for preventive purposes in clinical practice. There are numerous data in the Soviet and foreign literature indicative of the successful use of dibazol as a pharmacological prophylactic agent. It was noted that preventive intake of dibazol lowers the incidence of acute respiratory infections by 18% and related absenteeism by 35% [12]. A. M. Kapitanenko, who used dibazol during an epidemic outbreak of influenza in an organized group [3], and V. I. Semenov, who observed a beneficial effect with the drug at the early stage of adaptation to new climate conditions [10] cite analogous data. Experience with dibazol for vestibular disturbances [5] is of great interest to aviation and space medicine. These and other data prompted us to investigate the effect of dibazol on nonspecific resistance of individuals who work for long periods of time in pressurized premises on the ground or in flight. Evaluation of the effect of dibazol on defense functions of the body and biological significance of the drug in physiological mechanisms of human adaptation to such conditions had not been made previously.

## Methods

The studies were conducted on healthy men 25-32 years of age, whose activities for 2 months were limited to sealed rooms and were characterized by the high tension of operator work, hypokinesia, normal gas composition of air and uncomfortable microclimate parameters. The main group consisted of 8 men who took dibazol regularly in a daily dose of 5 mg. A total of 32 tests were made. The control group (24 men) took placebo, and we adhered to the principle of a double blind control. The studies were conducted 1 month before start of work under the above conditions, 15th day, after 1 and 2 months of work.

In all cases, we examined the morphological composition of peripheral blood, nonspecific defense factors of cells, antibacterial resistance of integument, physical work capacity and subjective state. The set of investigative methods included a leukocyte count, peripheral blood leukogram [6], intensity of leukocytolysis [11], adhesiveness of leukocytes, absorptive and digestive function of phagocytosis [8], automicroflora of the skin [4] and tolerance to a physical load [1].

## Results and Discussion

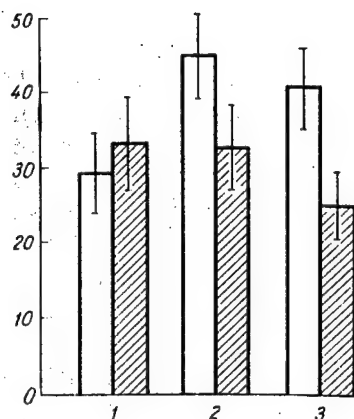
It was established that the dynamics of nonspecific constitutional resistance in sealed rooms differed in subjects given dibazol from the control. Intake of dibazol prevented a decline of defense potential of the body. Not only the physiological nature of changes in the body's defense functions throughout the investigation, but stable dynamics of adaptation processes at its end (see Table) were indicative of the efficacy of this agent. In essence, parameters of peripheral blood, cellular element of nonspecific defense and antimicrobial resistance of the integument did not change in subjects taking dibazol throughout the study period, and after 2 months the integral parameters of resistance even improved. In particular, there was 22.8% increase in efficiency of intracellular digestion, 29.2% decrease in bacterial contamination of the integument, which is indicative of increase in constitutional resistance to bacteria (see Figure).

Effect of dibazol on parameters of nonspecific resistance (M $\pm$ m)

| Dibazol intake, day | Subject group | Absorption capacity of leukocytes, RU (relative units) | Intensity of phagocytosis, RU | Phagocytic reaction, RU | Adhesiveness of leukocytes, % |
|---------------------|---------------|--|-------------------------------|-------------------------|-------------------------------|
| Background          | Control       | 21,24 $\pm$ 2,46                                       | 0,74 $\pm$ 0,06               | 0,84 $\pm$ 0,12         | 7,20 $\pm$ 1,29               |
|                     | Main          | 27,92 $\pm$ 4,74                                       | 0,82 $\pm$ 0,14               | 0,79 $\pm$ 0,09         | 7,89 $\pm$ 1,37               |
| 15                  | Control       | 18,60 $\pm$ 1,71                                       | 0,56 $\pm$ 0,06*              | 0,88 $\pm$ 0,06         | 11,32 $\pm$ 1,04*             |
|                     | Main          | 26,60 $\pm$ 4,19                                       | 0,82 $\pm$ 0,13               | 0,53 $\pm$ 0,14         | 7,38 $\pm$ 2,11               |
| 30                  | Control       | 14,46 $\pm$ 1,37*                                      | 0,51 $\pm$ 0,04*              | 1,12 $\pm$ 0,15         | 11,68 $\pm$ 1,09*             |
|                     | Main          | 25,54 $\pm$ 3,92                                       | 0,76 $\pm$ 0,08**             | 0,57 $\pm$ 0,07**       | 7,0 $\pm$ 1,87                |
| 60                  | Control       | 10,86 $\pm$ 1,24*                                      | 0,45 $\pm$ 0,03*              | 0,91 $\pm$ 0,09         | 11,36 $\pm$ 0,84*             |
|                     | Main          | 25,09 $\pm$ 2,54**                                     | 0,85 $\pm$ 0,14**             | 0,61 $\pm$ 0,09         | 7,50 $\pm$ 0,62**             |

\*P<0.05, as compared to background.

\*\*P<0.01 between groups.



Quantitative composition of deep cutaneous microflora before intake of dibazol (1), on 15th (2) and 60th (3) days of intake

White bars--placebo;  
striped--dibazol

At the same time, the subjects taking placebo presented an unfavorable direction of dynamics of parameters of defense functions. Already after 2 weeks, this group of subjects showed 24.3% decline in intensity of phagocytic reaction and substantial increase ( $P < 0.05$ ) in number and adhesiveness of leukocytes. All of the subjects with deadaptation changes in resistance parameters complained of rapid fatigability and decrease in work capacity. Objectively, this was confirmed by change in tolerance to physical load, the parameters of which declined at this time ( $P < 0.025$ ).

Thereafter, along with reliable decline of absorptive function of leukocytes and increased microbial contamination of the integument, more than half the subjects in the control group presented impairment of digestive function of phagocytes. Such

dynamics of defense functions are indicative of adaptation in the nature of a stress reaction [2], which is associated with decline of nonspecific resistance of the body. As a result, by the end of the study the parameters of defense functions were 1.5-2 times lower in the control than in subjects taking prophylactic doses of dibazol.

In summing up the foregoing, it is important to stress that dibazol has a combined effect on physiological functions of man. It enhances substantially general resistance to adverse factors and improves the subjective state. A positive pharmacodynamic effect of dibazol is observed after 10-15 days, and it is manifested by a combined effect on phagocytosis, blood homeostasis and antimicrobial resistance of the integument. At this time, there is improvement of general wellbeing and increase in tolerance to physical load, the level of which was 13-21% higher throughout the test period than in the control ( $P < 0.05$ ).

The results of individual analysis of the adaptation process, which was made on the basis of the prognostic criteria developed by I. A. Sapov and V. S. Novikov [9], indicate that dibazol has a beneficial effect on nonspecific mechanisms of adaptation. With intake of this agent, the adaptation process was satisfactory in all subjects, while no signs of deadaptation, premorbid states or disease were noted. At the same time, 12 subjects in the control group presented unsatisfactory course of adaptation, while 5 developed diseases of infectious and inflammatory genesis.

The submitted data are indicative of the positive effect of dibazol on nonspecific resistance of man under extreme conditions, which enables us to conclude that it would be desirable to use it as an activating and conditioning agent for individuals working under specific environmental conditions.

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EFFECT ON SEEDS OF HEAVY CHARGED PARTICLES OF GALACTIC COSMIC RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 27 Jun 83) pp 71-74

[Article by Ye. N. Maksimova]

[English abstract from source] The experiments were carried out on *Lactuca sativa* seeds exposed for 20, 66, 123 and 308 days in a biostack also containing physical detectors of heavy charged particles. The purpose of the experiments was to measure the yield of aberrant cells and its dependence on the exposure time and the site where particles hit the object. The cytogenetic examination demonstrated a significant difference between the seeds that were or were not hit by heavy charged particles. This is indicative of a significant contribution of galactic cosmic radiation to the radiobiological effect. The yield of aberrant cells as a function of the localization of heavy charged particles in the seed was established. The most sensitive target was the root meristem.

[Text] Investigations in space of the biological effects of heavy charged particles (HCP) during long-term flights (1 or more years) can be pursued only on model air-dry systems with delayed metabolic processes. For this reason, all of the experiments performed thus far by Soviet and foreign researchers used seeds, crustacean cysts and bacilli. In the studies pursued aboard craft of the Apollo type, artificial earth satellites (AES), Cosmos-782 and Cosmos-936, impairment of vital functions was found in cysts of *Artemia salina* and depression of growth in *Bacillus subtilis*; there was an elevated level of mutagenesis; cells were found with several aberrations rather than one per cell in seeds of *Lactuca sativa*. Such effects had also occurred in experiments where biological objects were exposed to protons and  $\gamma$ -rays in doses of several hundred rad. As a rule, the dose levels recorded in flight did not exceed a few rad. Consequently, the effects observed in the flight experiments could not be attributed to protons, which make up 85% of the flux of cosmic particles. It can be assumed that the observed effects are due to solid ionizing cosmic radiation, in particular, isolated charged particles. When HCP pass through biological tissue, in the track region of 20-200 Å there can be release of energy equivalent to a dose of one to several rad. Since release of energy from a heavy particle is strictly localized, the observed effects can be attributed to damage to

individual sensitive cellular structures. For this reason, it is important to study the effects of single hits by heavy ions on the cellular level in assessing the radiation hazard of spaceflights, particularly those of long duration, when HCP flow may be significant.

Our objective here was to obtain statistically reliable data on the yield of aberrant cells as a function of HCP hits in seeds during a flight experiment, as well as of topography of their passage through objects and flight duration.

#### Methods

The studies were conducted on seeds of *Lactuca sativa* lettuce flown aboard Cosmos-1129 for 19 days and the Salyut-6 orbital station for 66, 123 and 308 days.

The seeds were placed in biostacks that consisted of layers with seeds alternating with plastic detectors to record the tracks of heavy charged particles [1]. There were also thermoluminescent dosimeters in these stacks, which were used to record cumulative dosage. The seeds were attached with polyvinyl chloride alcohol in a single layer on a plastic sheet. Seeds through which heavy particles had passed were recorded upon combined examination of the layer with seeds and adjacent detectors. A team of physicists headed by A. M. Marennyy processed the detectors and did the scanning. Use of track detectors made it possible to differentiate the effect of HCP from the entire set of spaceflight factors (SFF). After scanning, seeds in all variants were soaked in tap water, allowed to germinate, seedlings were fixed and stained by the conventional technique for temporary aceto-orcein preparations. Upon microscopic analysis of the preparations we took into consideration all types of structural aberrations of chromosomes.

In order to pinpoint the site of HCP hit in the seed, a histological section of salad seeds was made and sensitive

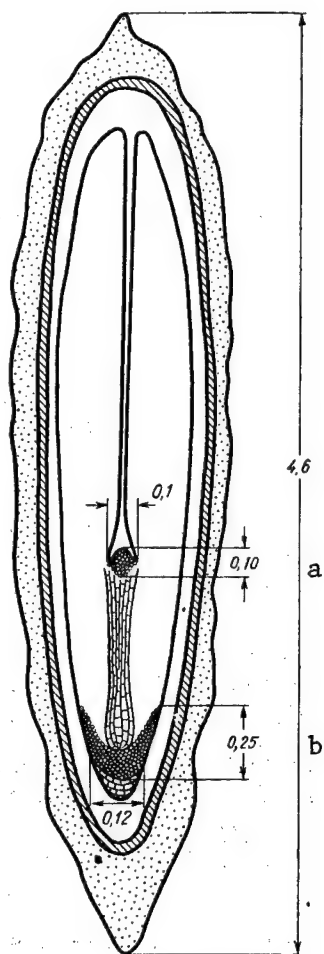


Figure 1.  
Dimensions (in mm) and location of sensitive structural elements of *Lactuca sativa* seeds

a, b) stem and root meristems, respectively

structures were identified: stem and root meristems (Figure 1).

## Results and Discussion

Figure 2 illustrates data on cytogenetic analysis of seedlings flown aboard AES Cosmos-1129 and Salyut-6 orbital station.

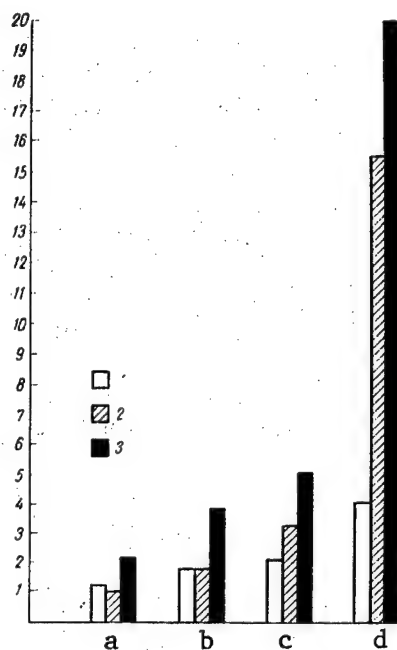


Figure 2.

Yield of aberrant cells in *Lactuca sativa* seeds flown aboard AES and orbital station

Y-axis, cells with chromosomal aberrations (%); x-axis:

a) Cosmos-1129 (20-day exposure; 3.7 cm<sup>2</sup> fluence)

b,c,d) Salyut-6--Soyuz (66-, 123- and 308-day exposure; fluence 8.5, 10.5 and 34.0, respectively)

1) control

2) flight (background)

3) flight with HCP

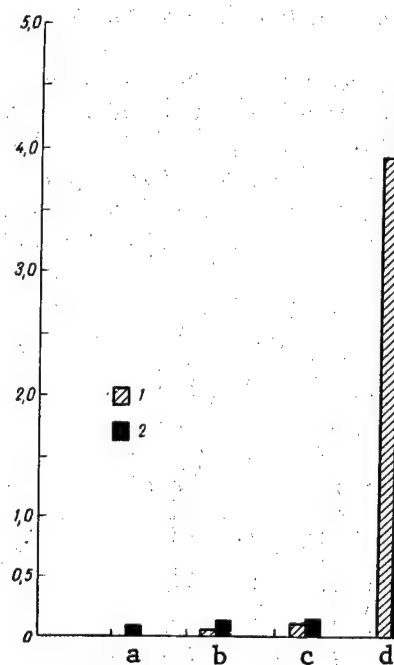


Figure 3.

Yield of cells with multiple chromosome aberrations in seedlings of *Lactuca sativa* flown aboard AES and orbital station

Y-axis, cells with multiple chromosome aberrations (%); x-axis:

a) Cosmos-1129 (19-day exposure)

b,c,d) Salyut-6--Soyuz (exposure for 66, 123 and 308 days, respectively)

1) flight (background)

2) flight with HCP

It should be noted that there was a different level of spontaneous mutagenesis in control seeds, which is related to natural seed aging.

A comparison of data for control and flight variants without exposure to HCP failed to demonstrate differences in yield of aberrant cells with 20- and 66-day exposure; there was an insignificant difference with 123-day exposure and substantial difference with 308-day exposure. The absence of differences and unreliability of yield of aberrant cells with 20- to 123-day exposure are indicative of insignificant influence of negligible ionizing radiation and other spaceflight factors.

As for flight seeds exposed to HCP, here we observed an increase in percentage of aberrant cells in all variants, as compared to parameters of flight seeds not affected by HCP and control seeds. Maximum yield of aberrant cells was observed with 308-day exposure. The unreliability of differences between values for flight seeds affected or unaffected by HCP with such long exposure is attributable to accumulation of the effects of various spaceflight factors, including ionizing radiation.

It should be noted that all aberrant cells in seeds were represented by a single aberration per cell; however, in the flight variants we encountered cells with two or more aberrations, so-called multiple aberrations. Figure 3 illustrates the yield of cells with multiple aberrations only in the flight variants. Such aberrations were absent in the control variants. The highest percentage of cells with multiple aberrations were observed in all experiments with seeds affected by HCP, and it rose with increase in exposure time. There was a high percentage of cells with multiple aberrations in seeds unaffected by HCP, particularly in the case of 308-day exposure, which indicates once more that there is increase in background dosage of ionizing radiation.

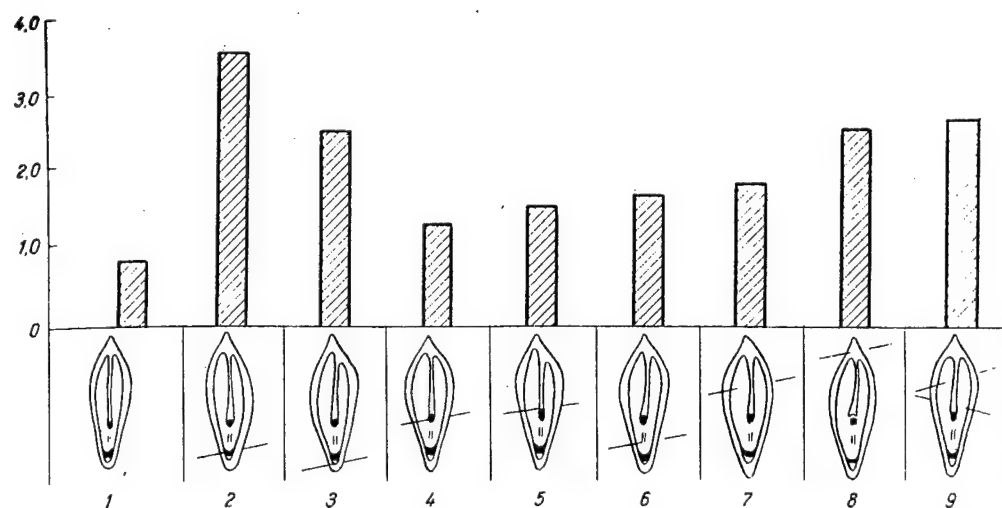


Figure 4. Yield of aberrant cells as a function of HCP hit site in *Lactuca sativa* seeds flown aboard Cosmos-1129 AES. X-axis, site of HCP hit in seed; y-axis, cells with chromosomal aberrations (%)

- |                          |                          |              |
|--------------------------|--------------------------|--------------|
| 1) no hit                | 4) stem meristem         | 7) cotyledon |
| 2) root meristem         | 5) next to stem meristem | 8) seed coat |
| 3) next to root meristem | 6) hypocotyl             | 9) two hits  |

Examination of each seed individually with exposure aboard Cosmos-1129 AES for 20 days revealed that the yield of aberrant cells did depend on the site of HCP hit in the seed (Figure 4). In the experiments aboard Salyut-6 orbital station lasting 66, 123 and 308 days, this function was not determined due to the insufficient amount of biological material affected by HCP. Figure 4 shows that the region of the root meristem is the most sensitive target, as

was suspected. Similar values were demonstrable when TCP hit the zone next to the root meristem and in the case of hits by two particles in a seed.

Integral doses constituted 0.4 to 3.5 rad with exposure time of 20 to 308 days.

Thus, as a result of conducting studies with different flight duration, we established that the yield of aberrant cells was a statistically reliable function of HCP hits in seeds, which indicates that the heavy component makes some contribution to the biological effect.

We established that the yield of aberrant cells is a function of localization of HCP in the seed.

Our findings are quite consistent with the results of studies conducted aboard Apollo spacecraft and Cosmos-type AES, where different reactions and degrees of biological damage to analogous systems were reported: total destruction, deformation, retarded development, mutations and various abnormalities [1-3]. We also found a distinction to the biological effect of HCP: distinct influence on long-term effects and no influence on germination of seeds, spores. In the experiments conducted aboard Cosmos-936 AES and Apollo-Soyuz project, anomalies were discovered that had not been encountered previously, either in other flight experiments nor experiments on a heavy-particle accelerator. Such abnormalities include rootlet splitting in seedlings and chlorophyll mutations in the form of yellow bands on corn leaves [4]. The ambiguity of data obtained in different studies can apparently be attributed to the fact that effects were evaluated without consideration of the HCP hit site in the target.

The doses recorded in all flight experiments were low, which was inconsistent with the results. Thus, the effect obtained with 308-day exposure of seeds corresponded to the one obtained with exposure of seeds to protons in a dosage of 0.5 krad and  $\gamma$ -rays in a dosage of 1 krad. Apparently, the dose concept generally used in radiobiology is not applicable to quantitative interpretation of the biological effect of HCP. The fact that there is a particle hit, with quantitative consideration of transferred energy could be a more adequate criterion in evaluating the "yield" of biological reaction per particle.

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## METHODS

UDC: 629.78:612.275.1-08

### MONITORING DOSAGE OF VOLATILE COMPOUNDS IN TESTS AT LOW BAROMETRIC PRESSURE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 22 Nov 83) pp 74-76

[Article by A. V. Sedov and V. I. Akimov]

[Text] When working in some types of airtight spaces, including insulated protective gear, man is exposed to the combined effect of such specific factors as low barometric pressure and hyperoxic gas atmosphere. These factors, which produce an additional burden on man, could aggravate the toxic effect of chemicals contained in the gas atmosphere of pressurized areas. For this reason, hygienic standards elaborated without consideration of the specific distinctions of man's work under such conditions cannot be extended to the gas environment of various pressurized areas.

Previously [4, 6, 7], studies were conducted with use of a device for dynamic gas mixing in order to validate the maximum allowable concentrations of such gases as carbon monoxide, methyl and dimethylamine. However, there are also volatile compounds (for example, phenol, benzene, toluene, ammonia and others) in the artificial atmosphere of pressurized areas, the monitoring of which is an important medical and engineering problem in the presence of low barometric pressure and breathing hyperoxic gas mixtures.

As a rule, microamounts of gases are diluted in a large volume of air in some container or other in order to measure them. G. Kh. Ripp [5], for example, used this method to validate the maximum allowable concentration (MAC) of divinyl.

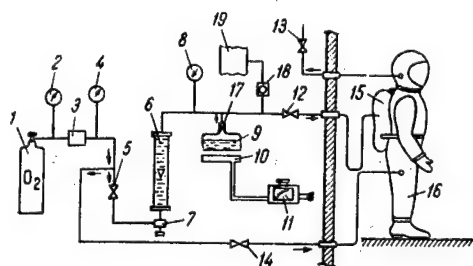
Another group of methods, which is based on the principle of measured additions of gases to air flow, is used for dynamic exposure of laboratory animals [1-3, 8] and in units for conducting tests on man [9, 10].

These versions of exposure chambers and devices, with which one can maintain a specific concentration of gases, are not suitable for studies to set the MAC of toxic agents for man when barometric pressure is low.

A dynamic gas-mixing unit [4], which is intended to control dosage of mixtures of carbon monoxide, methane and dimethylamine with oxygen, is the most suitable for the above-mentioned purpose. It is designed to provide for breathing at

low barometric pressure (to 198 mm Hg). However, the design of this unit did not permit testing in sealed spaces. Moreover, it was not intended to measure volatile compounds.

In view of the foregoing, a special device was developed, which permits measurement of toxic volatile agents (for example, phenol, acetone, ammonia, benzene, toluene and others) in oxygen. The Figure illustrates the schematic diagram of the apparatus. Oxygen is delivered at a pressure of  $150 \text{ kg/cm}^2$  from tank 1 to pressure regulator 3. Oxygen pressure in the tank is monitored by means of pressure gage 2. Then oxygen pressure is reduced by the regulator to  $10 \pm 2 \text{ kg/cm}^2$ , and pressure is monitored on gage 4. The oxygen is then distributed in



Apparatus for monitoring gases.  
Explained in the text.

two lines, one of which provides for emergency purging of the space under the suit and helmet when valve 14 is opened; the other serves to form and deliver a mixture of oxygen and fumes of the toxic volatile agent into the sealed space of the life-support system and isolation gear. When valve 5 is opened, oxygen is delivered to throttle valve 7, with which the required rate of oxygen delivery is set, and it is monitored with flowmeter 6. Check valve 12 must be open. After passing through the flowmeter, oxygen enters a duct, in which it is saturated with fumes of the

volatile agent contained in reactor 9. The saturated gas mixture passes through the open valve, through the duct in the wall of the pressurized chamber and then enters the ventilating circuit of life-support system 15 through the umbilical cord. The ventilation system is connected by input and output umbilical cords to insulating gear 16. In this case, the oxygen of the apparatus is merely a vehicle to deliver toxic volatile agents into the space under the suit and to the respiratory zone. The main supply of oxygen needed to assure vital functions and replace any possible leaks is located either in tanks of life-support system 15 or onboard oxygen supply systems. Metering and the required concentration of volatile agents in the space under the suit are achieved by changing oxygen delivery in the apparatus, as well as by warming the reactor with heater 10. Heater temperature is set using voltage regulator 11. Thus, the concentration of volatile toxic agents in ventilated space of the insulating gear is a function of oxygen delivery by the apparatus and heater temperature. It is easy to obtain these functions by means of preliminary calibration.

In some cases (for example, during long-term tests of isolating gear or absorber of life-support system), in order to improve the performance of the apparatus, increase its reliability and stability of delivery of gas mixture at constant temperature and pressure, it is possible to use interchangeable reactors 9 with different evaporation surfaces. In this case, nozzles 17, which are installed at the output of the reactor, can play this part. By experimentally selecting nozzles with different bores in one or several reactors with different evaporation surfaces, one can obtain several devices that permit delivery of measured amounts of volatile agents to the respiratory zone and under the suit.

The apparatus is equipped with safety valve 18 and flexible reservoir 19 to assure safe operation. When valves 7 and 12 are closed, gas pressure could rise above the nominal (or set) level in part of the line between them and the reactor. In this case, the safety valve is actuated and surplus gas is collected in the flexible reservoir.

Both technical and medical-technical tests can be run with the apparatus. In both cases, gas mixtures can be delivered continuously and discretely in low and high concentrations. During technical testing it was found that the device is simple, reliable and convenient to operate.

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## DETERMINATION OF INDIVIDUAL TOLERANCE TO HYPERBARIC OXYGEN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 5 Aug 83) pp 76-77

[Article by G. L. Zal'tsman, G. A. Kuchuk and A. N. Rovnyy]

[Text] A hyperbaric gas and water environment, as a special environment of man, is characterized by the presence of many extreme factors (high ambient and partial gas pressure, density and heat conductivity of medium, etc.). Under such conditions, human labor is considered to be particularly heavy, dangerous and deleterious. For this reason, screening individuals with tolerance to extreme factors of a hyperbaric environment is of paramount significance in order to improve the safety and efficiency of underwater work.

Among the most important extreme factors of a hyperbaric environment, we must mention the effect on man of high partial pressure of oxygen and neutral gases, nitrogen and helium. These factors, which have a marked neurotropic action, limit the depth of submersion and exposure time, whereas for individuals with high predisposition they could be threatening even in the range that is accepted for work. Appearance of early manifestations of pathological reactions was used to determine individual tolerance to the above extreme hyperbaric factors.

Man encounters high partial tension of oxygen, which is a mandatory component of breathing mixtures, in virtually all cases of exposure to a hyperbaric environment, whereas in the range of low pressure (up to 0.2 MPa) pure oxygen is used for breathing. Investigations of the toxic effect of high oxygen pressure has more than a 100-year history. In the classical work by P. Ber [2], the acute convulsive form of oxygen intoxication was established. Clinically, it is manifested in the form of attacks of tonic-clonic seizures that cannot be distinguished from epileptic ones. Formation of oxygen epilepsy depends on both magnitude of pressure and exposure time. The earliest symptom is trismus of muscles, face or functioning organs. Then, as time of exposure to high pressure increases, there is development of myoclonia of remote muscle groups that turns into a generalized attack. As shown by investigations [2], development of these somatic manifestations is inherent in pressure in excess of 0.3 MPa. At lower pressure, as a rule there are autonomic disturbances related to spasm of smooth muscles of vessels, bronchi, etc.

Use of instrument tests made it possible to demonstrate two types of changes and disturbances that man develops when exposed to high oxygen pressure. The first type is referable to early changes: decline of critical frequency of optic and auditory stimuli and qualitative changes in succession of patterns. However, it was not possible to establish a correlation between the dynamics of these residual processes in the central nervous system and subsequent development of symptoms of toxic effect of oxygen. The second type refers to changes in bioelectrical activity of the brain, muscles and hemodynamic disturbances. They develop virtually concurrently with formation of the clinical reaction. Thus, it has not been possible thus far to find reliable instrumentation methods to predict development of oxygen epilepsy.

While the general reaction to hyperbaric oxygen is similar, there are considerable individual differences in time of formation of the reaction: from 6 to 96 min at pressure of 0.37 MPa [3], from 71 to 227 min at 0.3 MPa and from 6 to 84 min at 0.4 MPa [2]. Among divers there are individuals with high individual predisposition to the effect of oxygen, since medical screening does not pick up those individually susceptible to the effect of oxygen under pressure. A case has been described of significant narrowing of fields of vision during oxygen decompression in the conventional modes [2].

The foregoing warrants the conclusion that it is a rather pressing task to develop methods of specific screening according to individual susceptibility to the toxic effect of oxygen.

#### Methods

The method of determining individual tolerance to hyperbaric oxygen consisted of the following: determination of mode of oxygen compression eliciting formation of response with marked and objective early manifestations at the optimum time for conducting tests; development of clinical and instrumentation methods of demonstrating parameters of the subject's condition; setting standards for the obtained parameters for screening purposes.

To perform the tasks set forth, we used pressure of 0.2 MPa with exposure time of 1.5 and 2 h and 0.25 MPa with 1-h exposure. Pressure was generated in the chamber with compressed air, while the subjects breathed oxygen using individual gear. Oxygen content in the breathing sac (according to gas analysis) was held at an 80% level and, consequently, partial oxygen pressure was 0.24 and 0.28 MPa, which conforms to the permissible norms of oxygen pressure for man. During compression, each subject was under constant observation by both the support diver in the chamber and support physician. In addition, we used the following methods: determination of fields of peripheral vision, electroplethysmography (EPG) of the index finger, recording of galvanic skin response (GSR) and quasistable difference in potentials (QSDP) [1]. In all, there were 70 man-dives: 16 at pressure of 0.2 MPa and 54 at 0.25 MPa.

#### Results and Discussion

Exposure to pressure of 0.2 MPa failed to demonstrate marked objective or subjective changes in the subjects' condition. For this reason, we used a pressure of 0.25 MPa in subsequent tests. While exposed to this pressure,

5 subjects developed early signs of the toxic effect of oxygen in the 12th-30th min: intense arrhythmic breathing, myoclonia of some muscle groups (with partial generalization in 1 subject). Prompt disconnection of the equipment and change to breathing with compressed air caused the symptoms to regress. No marked changes in wellbeing or health status occurred in the rest of the subjects throughout the exposure period. Use of the perimetry method failed to demonstrate changes in most subjects, while occurrence of changes in some cases was in the direction of improvement of parameters. Electroplethysmograms of all subjects showed bradycardia and diminished amplitude of pulse waves, which are inherent in the effect of oxygen at high pressure. As a rule, the GSR and QSDP parameters rose in all subjects by the end of the period of exposure to 0.25 MPa (45th-55th min). In subjects who displayed increased susceptibility to oxygen, the dynamics of EPG, GSR and QSDP parameters did not differ from those of the other subjects. Thus, only the clinical method is a reliable indicator of development of reactions to high oxygen pressure. We failed to find reliable instrumentation methods of testing the toxic effect of oxygen.

The results of our studies revealed that subjects with individual predisposition to the effect of hyperbaric oxygen differed appreciably from the rest, since they developed an epileptic reaction in the 12th-30th min, whereas the other subjects did not present changes during 1-h exposure to the same pressure. In addition, on the basis of data obtained in previous studies [2], one could expect that the changes developing in the course of further exposure would be in the form of autonomic disturbances, whereas in susceptible subjects we found somatic disturbances.

Thus, it can be concluded that the developed screening methods permit detection of individuals with low tolerance to hyperbaric oxygen, on the basis of the early clinical manifestations of the body's response. According to the data obtained, the number of such individuals constitutes about 8%. Further refinement of the methods for screening individuals with low tolerance to oxygen according to parameters of EMG, EPG, ECG and others is theoretically possible; however, the rapid development of the reaction will probably require use of computer processing of obtained data.

Direct methods of specific screening for individual tolerance to hyperbaric oxygen may be supplemented with indirect ones, that do not require reproduction of high pressure. Such methods include physiological factors such as hypoxia, pharmacological agents, fine biochemical indicators of differences in individual reactions. The indirect methods must be a continuation of direct screening methods, their next stage. High correlation with indicators of direct screening methods is a mandatory prerequisite for development and use of indirect methods of specific screening.

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DEVELOPMENT OF INTERACTIVE DATA PROCESSING SYSTEM IN PSYCHOLOGICAL ENGINEERING STUDIES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 14 Oct 83) pp 78-81

[Article by I. G. Nidekker, A. P. Nechayev, Ye. Ye. Brodetskaya, A. V. Zarovnyy, B. N. Ryzhov, V. A. Stepanov and G. I. Odínokov]

[Text] A typical distinction of man-machine system studies is that large volumes of heterogeneous information are received, which include psycho-physiological, engineering psychological, technical and other indicators, analysis of which (by virtue of their great variability and uncertainty) presents difficulties. For this reason, automation of scientific research on engineering psychology as, incidentally, in other branches of science, is an important practical task. However, it is still premature to automate engineering psychological or biomedical experiments that take into consideration the element of control (as, for example, in automation of industrial processes), since the large number of often interrelated processes studied at the same time, their low stability, poor reproducibility and other factors have a negative effect on reliability of decision making. This is why, the main task at this stage is to automate the performance of investigations, starting with gathering and processing data on a real time scale and ending with display of results in a form that is convenient to interpret.

All this imposes certain requirements as to the structure of the automated data processing system. While some advances have been made in the area of standardization at the stage of measuring biomedical parameters (for example, development of conjugation means in the KAMAK standard [3]), standardization of experimental methods, procedures and modes of processing, interpretation and display of data presents major difficulties at this time. Effective solution of the problem of standardization and unification in medicine implies automation of input and processing of experimental information, development of methods of visualizing it and data banks. This approach permits analysis of large, homogeneous and representative (from the standpoint of both logic and occupation, and statistics) samples, increases the informativeness and reliability of results.

Although the automated system solves concrete problems in each experiment and its performance is determined by technical capabilities [1, 2, 4, 6, 7], it should nevertheless satisfy several general requirements. The main ones

are to provide for gathering any form of experimental data (analog signals, qualitative and quantitative information), reduce processing time, constant visual monitoring, possibility of immediate change in experimental conditions, output of results in a form that is convenient for the experimenter, feasibility of accumulation and long-term storage of information.

We shall discuss here a system of automating research in engineering psychology for investigation of the distinctions of operator performance in the mode of compensatory tracking. The system inputs in the computer on a real time scale the physiological information and features of operator work, puts out directly the results of calculating given parameters, as well as records information on magnetic medium in order to accumulate it and then process it on an expanded program.

Figure 1 is a block diagram of the system. Preliminary conversion of information (amplification, filtration, scaling, etc.) is effected with an MN-10 analog computer. In our study, seven parameters were used: heart rate (HR), respiration rate (RR),  $\beta_2$ - and  $\Theta$ -waves of electroencephalogram (EEG), phase component of galvanic skin response (GSR), electromyogram (EMG) and modulus of tracking error, although in the general case the quantity is limited only by the characteristics of the communication channel.

Before starting each test, identification data about the operator, scalar and calibration coefficients, quantization interval to convert analog information to digital and all information about experimental conditions (range of changes in parameters, intervals at which dynamic characteristics are obtained, code words to control data processing programs, set of formulas used for calculations, etc.) are fed into the computer. In the course of the studies, phrases are fed into the computer that reflect progress of the experiment. These phrases, along with the results of calculations and operator data subsequently form the experimental protocol.

The automated complex for input, accumulation and mathematical processing of information within the limits of the described system operates in the two following modes" 1) in the mode of "express [immediate] evaluation," when data coming to the computer from the operator's work place are processed on a real time scale and the results are relayed to the experimenter on a video monitor (see Figure 1), and all data inputted from the display in the dialog mode is stored on magnetic medium. In the "express evaluation" mode, the minimum number of parameters is furnished to the experiment, as necessary to assess the efficiency of operator performance. The set of such parameters depends on the purpose of the experiment and time in which the experiment wishes to obtain dynamic characteristics of the object; 2) "experiment protocol" mode, when data recorded on magnetic medium in the course of the study are subsequently processed on the computer on an expanded program (comparison of results, optimization of parameters, etc.). In this mode, results are put out in the form of texts and tables on the display screen, alphanumeric printer, as well as graph plotter.

In the course of operation, a file of base data and resultant parameters is produced. The system includes a package of statistical programs for analysis

and generalization of these data. It should be noted that an increasing number of works has appeared recently, in which dissatisfaction is voiced with the results of statistical processing of clinical and experimental material. The opinion is held that simple substitution of data in statistical formulas does not yield expected results and is "merely a means of translating experimental data into a form that is less convenient to interpret" [7]. For this reason, in developing the package of statistical programs we included as a mandatory condition the possibility of dialogue between the experimenter and the computer. The dialogue starts with visualization of base material on a display.

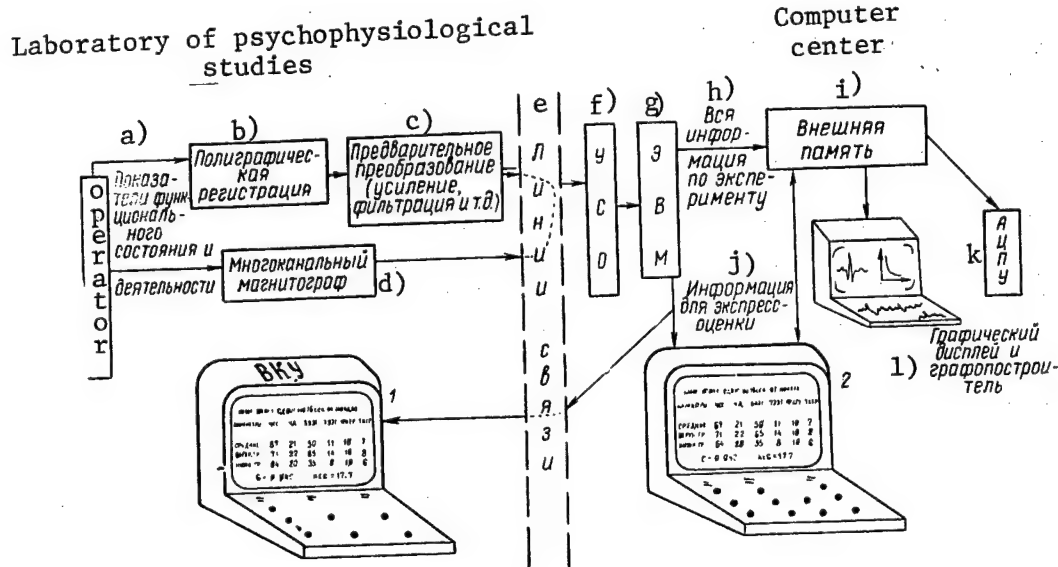
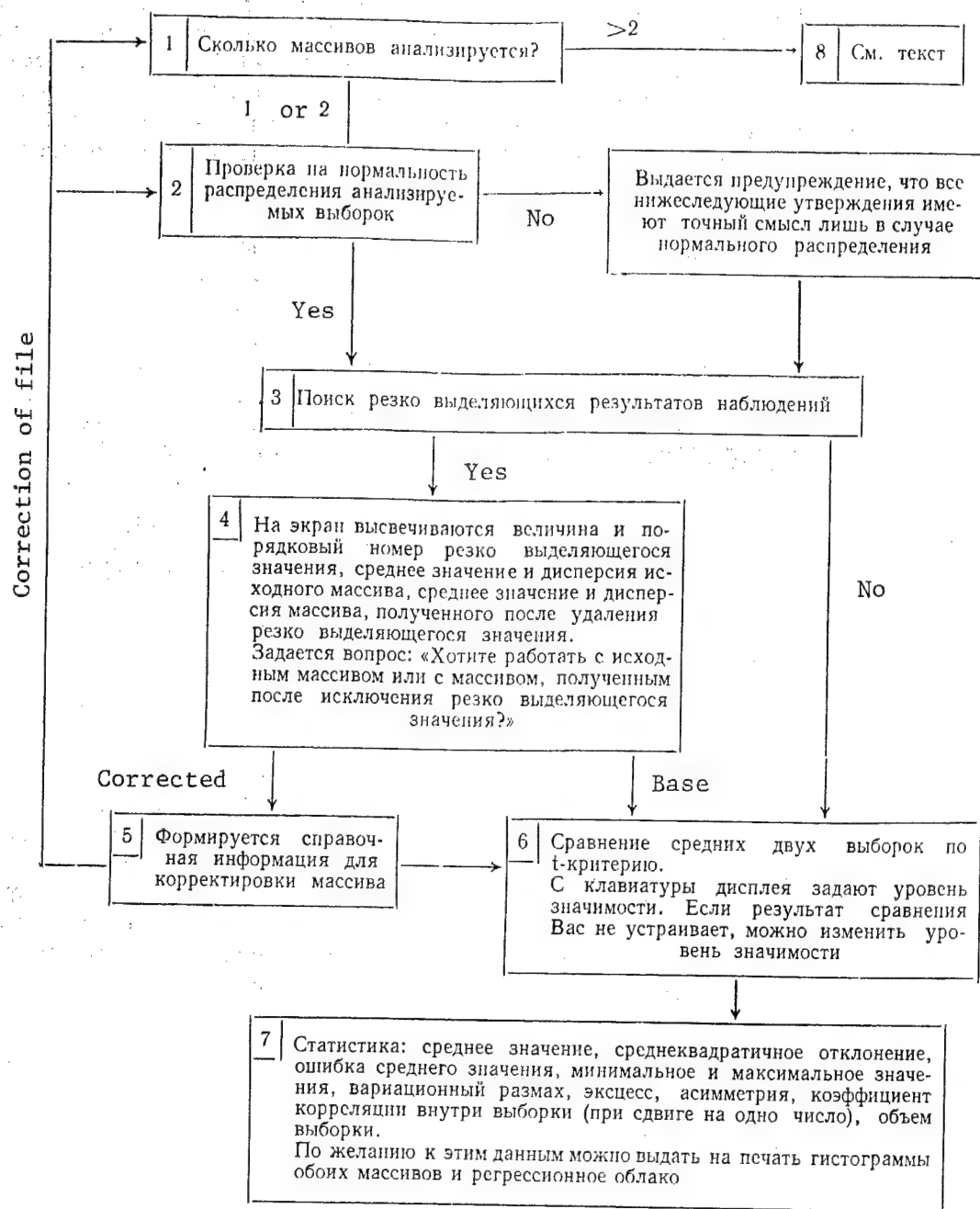


Figure 1. Block diagram of system for automation of studies in engineering psychology. The following information is put out on the screens of 1 (video monitor) and 2 (alphanumeric display) in the course of the experiment every  $\tau$  seconds ( $\tau$  is set by the experimenter): time from start of experimental mode used, titles of parameters (HR, RR, TEEG, etc.) and under them their mean values and standard deviations, integral parameter of operator efficiency

- Key:
- a) parameters of functional state and performance
  - b) polygraphic recording
  - c) preliminary conversion (amplification, filtration, etc.)
  - d) multichannel magnetograph
  - e) communication lines
  - f) interface
  - g) computer
  - h) all information about experiment
  - i) file
  - j) information for express evaluation
  - k) alphanumeric printer
  - 1) graphic display and plotter
  - BKY) video monitor

Block diagram of dialogue system for primary statistical analysis of file data accumulated as a result of operation of automated system



Key:

- 1) How many arrays analyzed?
- 2) Check for normal distribution of analyzed samples----Warning is issued that all statements below have precise meaning only in the case of normal distribution
- 3) Search for sharply outstanding observation results  
[continued on the next page]

Key (continued):

- 4) Value and sequence number of sharply outstanding value, mean value and dispersion of base array, mean value and dispersion of array obtained after removal of sharply differing value. The question is posed: "Do you wish to work with base array or array obtained after exclusion of sharply differing value?"
  - 5) Reference information is formed in order to correct file
  - 6) Comparison of averages of two samples according to  $t$  criterion. Level of significance given from display keyboard. If result of comparison is not what you need, level of significance can be changed
  - 7) Statistics: mean value, standard deviation, mean error, minimum and maximum values, range of variations, excess, asymmetry, coefficient of correlation within sample (with 1-number shift), size of sample. If so desired, histograms of both files and regression cloud [?] can be printed out
  - 8) See text
- 

In the block diagram of the dialogue system of primary statistical processing of results of observations, the programs of unit 8 operate on the principle of trying to find, "at any cost" ("cost" is level of significance), a difference between mean values of compared samples. It is known that if the computed  $t$  criterion\* is greater than tabular  $t(k, p)$  with a given number of degrees of freedom  $k$  and given level of significance  $p$ , the means of the two samples differ from one another and we could be wrong in  $p \cdot 100$  cases out of 100. In our program, with a given number of degrees of freedom  $k$ , we search for a level of significance  $p$  at which the calculated  $t$  criterion would be greater than tabular  $t(k, p)$ . In addition to the results of comparison by the  $t$  criterion ("yes-no" and level of significance), the following statistical parameters are put out for each sample: mean value and standard deviation, error of mean, minimum and maximum values, range of variation, excess, asymmetry, autocorrelation coefficient with first shift, size of sample. One uses unit 8 programs after correcting the file, when the experimenter is sure that his data conform to the requirements for statistical processing.

A package of programs was also developed to test the correlation between two samples. It permits finding the coefficient of correlation between these samples and then, in the dialogue mode, to evaluate the reliability of the obtained result. The correlation field (Figure 2) is flashed on the display, and the experimenter determines how many lines of regression can be drawn. The correlation field is broken down into subregions (there are 3 in Figure 2) with a light pen. The type of line of regression (linear or nonlinear to the appropriate power) is selected in the dialogue mode. As an illustration, Figure 2 shows a specially selected example where one can clearly see different functions, although in practice it is often difficult to definitely identify subregions. The program also has a criterion for checking the hypothesis of absence of correlation between the tested samples.

---

\*Two formulas were programmed to calculate the values of  $t$ : for small ( $N \leq 30$ ) and large ( $N > 30$ ) samples.

The developed system makes it possible to perform the following operations: 1) automate analysis of parameters of operator state and performance in real time; 2) change experiment modes at any time depending on current value of express evaluation; 3) process information using expanded programs; 4) accumulate files of experiments that could subsequently be used for more complex analysis. It is expressly this part of the system that contains vast possibilities with respect to assessing the adequacy of some formula or other used for calculations and functions, making a comparative analysis, determining informativeness of parameters, optimizing criteria, etc.

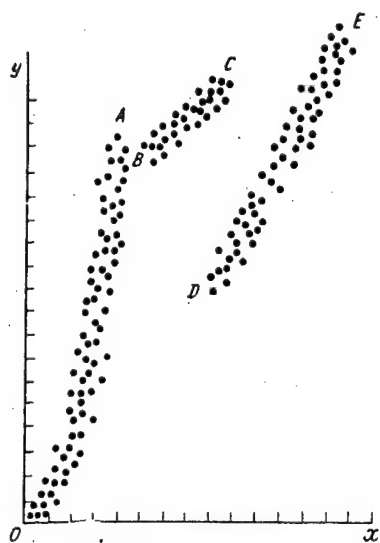


Figure 2.

Testing correlation between two sets  $\{x_i\}$  and  $\{y_i\}$

A fragment of statistical information about two samples is shown; here too, one usually furnishes two histograms, all statistical parameters listed in the text, coefficients of mutual correlation. On the illustrated "correlation field," we see that there are 3 functions over the entire range of analysis of correlation between the two samples.

If subregions OA, BC and DE were outlined with a light pen, we would have the following regression equations:

$y = x^2$  for OA,  $y = x + 10$  for BC and  $y = 2 \cdot x - 6$  for DE. If we search for a coefficient of correlation in region OE we could get false information about correlation between the two samples ( $r_{xy} = 0.34$ )

The automated system for conducting studies in engineering psychology expands significantly the capabilities of the experimenter. On the one hand, it relieves him of additional calculations and time-consuming manual processing of information, provides for a convenient form of logging experiments and, on the other hand, it makes it possible to obtain an immediate express evaluation of efficiency of operator performance in the course of the study, including both physiological and productive parameters. It should be stressed that we consider the proposed system for statistical analysis of information as the first phase in development of an interactive statistical package of programs that would enable us to determine the extent to which base data conform to requirements for statistical processing (type of distribution, homogeneity of sample, etc.). For this reason, the system in question has provisions for further upgrading of existing programs and development of new ones.

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## BRIEF REPORTS

UDC: 612.173.3-06:612.766.2]-088.53

### RESULTS OF ECHOCARDIOGRAPHIC STUDIES OF RESTING MACACA MULATTA MONKEYS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 9 Sep 83) pp 81-84

[Article by R. T. Kazakova, A. P. Yurenev, B. S. Kulayev, A. N. Nazin and Yu. V. Shevchenko]

[Text] The development of modern biology makes it imperative to use informative, noninvasive methods of assessing the structural and functional state of the heart for dynamic studies. Echocardiography is such a method [1, 2, 4]. However, only isolated reports have been encountered until recently in the literature concerning the distinctions of echocardiography on monkeys [3]. We were the first to investigate the distinctions of echocardiograms of *Macaca mulatta* (*Macaca rhesus*) monkeys at rest. The special interest in making echocardiographic studies of this monkey species is attributable to their use in space physiology.

Our objective was to use echocardiography to define standard parameters of central hemodynamics in resting *M. rhesus*.

#### Methods

Echocardiography was performed on 20 *M. rhesus* 3-4 years of age with average weight of 4.2 kg, under ketalar anesthesia (0.5 mg/kg weight). The echocardiogram of the left ventricle was recorded in the M mode, from the aorta to the apex along the long axis of the heart, using a Soviet Uzkar-3 echocardiograph on photographic film (2.7 MHz sensor) and the Echoview 80-C echocardiograph of the Picker firm (United States) on photosensitive paper (5 MHz sensor). The sensor was placed along the left edge of the sternum on the level of the 3d-4th intercostal space. Concurrently with the echocardiogram, we recorded the heart rate (HR). The measurements were taken on the level of the mitral valve chorda or on the level of visualization of the two cusps at the site of typical motion of the posterior wall of the ventricle and septum.

From the echocardiogram we determined the dimensions of the chambers of the left ventricle in systole ( $D_s$ ) and diastole ( $D_d$ ). The systolic size of the chamber was measured over the maximum approximation of structures of the posterior wall and septum (smallest intraventricular dimension). The diastolic size of the chamber of the left ventricle was determined by the descending arm

of the R wave. We calculated end systolic (ESV) and end diastolic (EDV) volumes of the left ventricle [7, 8] on the basis of data obtained using the formula,  $V = \frac{7.0}{2.4D} \cdot D^3$ , where V is volume of left ventricle and D is size of left ventricle. We calculated stroke volume (SV) using the formula,  $SV = EDV - ESV$ , ejection fraction (EF) by the formula,  $EF = SV/EDV$ , circulation volume (CV) by the formula  $CV = SV \times HR$  and degree of shortening of the anteroposterior size of the left ventricle in systole (% $\Delta S$ ) by the formula  $\Delta S = \frac{D_d - D_s}{D_d} \cdot 100\%$ . In addition, we determined the overall size of the heart, diameter of the aorta and size of the left atrium, thickness of intraventricular septum and posterior wall of left ventricle at the end of diastole.

## Results and Discussion

Ultrasonic scanning of the heart revealed that methodologically, it is more difficult to perform echocardiography on this species of monkeys than on man. This is attributable to the anatomical distinctions of their chest, narrow intercostal spaces, more vertical position of the axis of the heart, rotation of apex to the back, etc. Because of the high HR in the monkeys, mitral valve function is recorded in the form of a monophasic curve, i.e., there is virtually no phase of slow filling and the phase of rapid filling is immediately followed by atrial systole. It should also be noted that, unlike man, reduction in size of the left ventricle of monkeys during systole occurs more due to contraction of the interventricular septum. Echograms of the left ventricle and aorta recorded on different echocardiographs are illustrated in Figures 1-3. We should also mention another important methodological distinction when performing echocardiographic examination of monkeys. With the insignificant change in angle of the sensor needed to obtain echograms of the left ventricle, we see on the echogram a seeming lag in contraction of the posterior ventricular wall in systole in relation to contraction of the interventricular septum. Such a tracing of the echogram should be considered incorrect (Figure 4).

Proceeding from the anatomical distinctions demonstrated by this method of examination, it should be borne in mind that when working with monkeys weighing more than 5-6 kg, it is considerably more difficult to perform echocardiography. This is attributable to the fact that with increase in weight and age there is drastic change in configuration of the chest in monkeys. It is more expedient to use ultrasonic sensors at frequency of 5 MHz. Such sensors enhance resolution of the instrument and are generally used in pediatric practice.

Heart rate fluctuated over a wide range, 120-207/min, the mean being  $170 \pm 12$ /min. Overall size of the heart averaged  $3.6 \pm 0.04$  cm, diameter of the aorta was  $1.0 \pm 0.1$  cm and the left atrium was  $0.8 \pm 0.1$  cm in size. Left ventricular chamber in diastole was  $2.0 \pm 0.1$  cm in size and in systole  $1.5 \pm 0.1$  cm; end diastolic and end systolic volumes of the left ventricle calculated on the basis of the preceding data constituted  $12.7 \pm 0.7$  and  $6.0 \pm 0.6$  ml, respectively.



Figure 1. Echogram of monkey's left ventricle recorded with Echoview-80 echocardiograph of Picker firm (United States)

- |       |                                  |     |   |
|-------|----------------------------------|-----|---|
| МЖП)  | interventricular septum          | ЛЖ) | left ventricular chamber                          |
| ЗСЛЖ) | posterior wall of left ventricle | Э)  | endocardial surface of posterior ventricular wall |
| ЭКГ)  | electrocardiogram                |     |   |

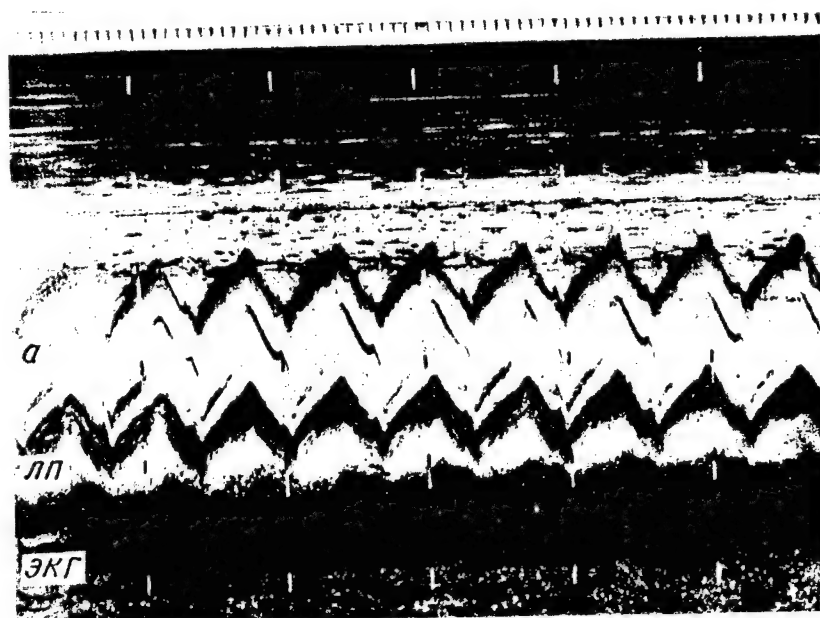


Figure 2. Echogram of base of monkey's aorta recorded with Echoview-80 echocardiograph, Picker firm (United States)

- |     |                |      |                   |
|-----|----------------|------|-------------------|
| α)  | lumen of aorta | ЭКГ) | electrocardiogram |
| ЛП) | left atrium    |      |                   |

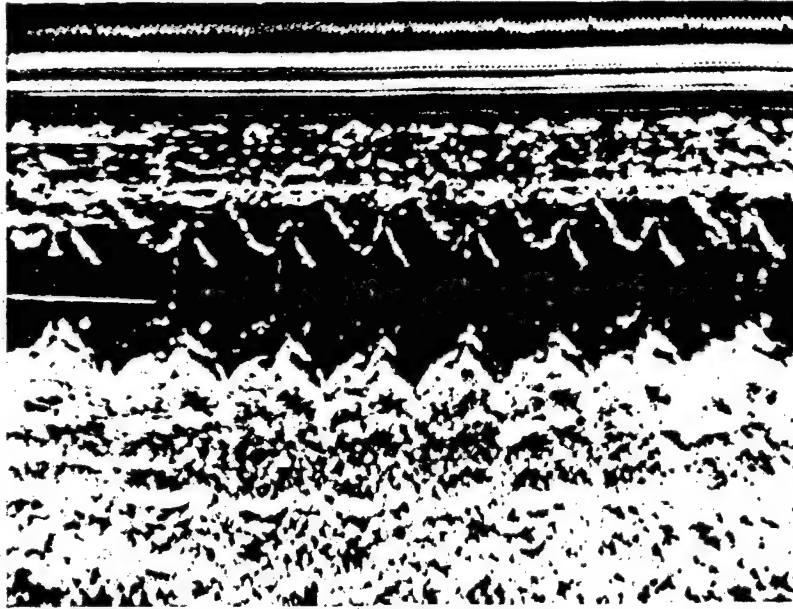


Figure 3. Echogram of monkey's left ventricle recorded on Uzkar-3 echocardiograph

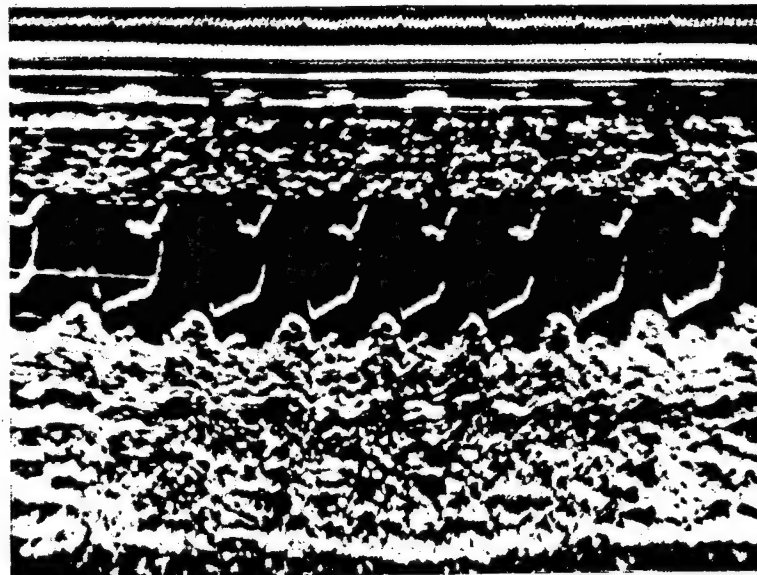


Figure 4. Incorrectly recorded echogram of left ventricle using Uzkar-3 echocardiograph

Stroke volume, which is the difference between end diastolic and end systolic volumes constituted in the 20 monkeys  $6.7 \pm 0.5$ , or  $1.6 \pm 0.2$  ml/kg weight, while CV was  $1139 \pm 126$ , or  $272 \pm 38$  ml/kg. Thickness of the interventricular septum and posterior wall of the left ventricle constituted  $0.4 \pm 0.03$  and  $0.6 \pm 0.02$  cm, respectively. Ejection fraction averaged  $54 \pm 3.4\%$ , while shortening of the anteroposterior size of the left ventricle in systole was  $27 \pm 2.3\%$ .

In the presence of elevated emotional status of monkeys, their individual distinctions and as a result of differences in testing conditions, one could expect considerable fluctuation of standard parameters of central hemodynamics obtained by other authors; however, our data are consistent with the results of testing this species of monkeys using the Fick method. Thus, according to some authors [6], mean HR was  $174 \pm 18$ /min in 8 monkeys with average weight of 5.3 kg under phencyclidine anesthesia. SV and CV averaged  $5.8 \pm 2.4$  and  $1070 \pm 300$  ml, respectively, in 14 monkeys weighing 5-6 kg. When scaled to 1 kg weight, our values for SV and CV coincide adequately with the data of these authors. According to other researchers [5], average SV for 21 monkeys was 7.5 ml, and CV was 1310 ml. However, these authors performed tests on nonanesthetized monkeys, which makes it difficult to compare results.

Thus, in this study we obtained standard parameters of central hemodynamics for resting monkeys and demonstrated that it is possible in principle to use the ultrasonic method to gain additional information about cardiovascular system function in this species when conducting experimental studies as related to problems of space physiology. Use of this method becomes particularly important as a verification of impedance rheoplethysmography on echocardiograms in view of the fact that impedance rheoplethysmography is apparently the most suitable for studies of cardiac function during unmanned spaceflights.

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## LIPOGENESIS IN RAT LIVER AFTER FLIGHT ABOARD COSMOS-1129 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 19 Aug 83) pp 84-85

[Article by L. Macho, R. A. Tigranyan, N. Skottova and M. Palkovic (CSSR and USSR)]

[Text] It has been established that there is weight loss, reduction of layer of fatty tissue in subcutaneous tissue and other fat reservoirs in animals as a result of spending 22 days in spaceflight aboard the Cosmos-605 biosatellite [5]. Tests conducted aboard Cosmos-605, Cosmos-690, Cosmos-782, Cosmos-936 and Cosmos-1129 biosatellites revealed that long-term exposure of rats to weightlessness is associated with changes in lipid metabolism [1-3, 4, 8]. The experiment aboard Cosmos-782 revealed considerable decrease in activity of the main lipogenetic enzymes--malic enzyme and ATP-citrate lyase--in the rat liver immediately after the flight. Activity of these enzymes did not differ from the control 26 days after the flight [6]. A decline in activity of liver malic enzyme and ATP citrate lyase was also demonstrated immediately after the flight in rats flown aboard Cosmos-936 in weightlessness, whereas those exposed to artificial gravity aboard the biosatellite showed no difference from the control in activity of these enzymes. Enzyme activity did not differ from the levels in the vivarium control 25 days after landing [7]. We are dealing here with an investigation of the activity of one of the key lipogenetic enzymes, malic enzyme, in the liver of rats flowing aboard Cosmos-1129, and we also intended to determine the rate of repair of previously found changes when the recovery period was shortened, as well as to test the effect of recurrent stress in the recovery period on changes in enzyme activity.

## Methods

We conducted tests with male Wistar SPF (Bratislava, CSSR) rats flown for 18.5 days aboard Cosmos-1129 biosatellite. The animals were decapitated 6-8 h after landing and on the 6th postflight day. Some of the animals sacrificed on L+6 were submitted to 5-fold immobilization stress (150 min per day), while others were not. The control and synchronous groups of rats were submitted to immobilization stress repeatedly. There were 6-7 animals in each experimental and control group.

The liver (1 g) was homogenized in 1 ml cooled 0.15 M KCl; the homogenate was transferred into centrifuge tubes, brought up to 4 ml with the indicated KCl

solution and centrifuged for 60 min at 40,000 r/min and temperature of 10°C. We measured the activity in supernatant of malic enzyme (L-malate:NADP-oxidoreductase, decarboxylating, EC 1.1.1.40) [9] and concentration of protein [10]. Statistical reliability was calculated using Student's criterion.

## Results and Discussion

Immediately after the experiment there was a decline in activity of malic enzyme in the liver of flight and synchronous groups of animals; however, this decline was reliable only in the synchronous control (see Table).

Malic enzyme activity (in  $\mu\text{mol NADP}\cdot\text{H}_2/\text{mg protein/min}$ ) in rat liver ( $M\pm m$ )

| Animal group           | 6-8 h after landing | L+6               | L+6 + immobilization stress |
|------------------------|---------------------|-------------------|-----------------------------|
| Vivarium control       | 859,8 $\pm$ 63,7    | 740,8 $\pm$ 59,5  | 572,8 $\pm$ 88,8            |
| Flight                 | 655,6 $\pm$ 103,2   | 458,0 $\pm$ 70,7* | 403,0 $\pm$ 61,6**          |
| Synchronous experiment | 487,4 $\pm$ 47,2*   | 534,3 $\pm$ 65,8* | 591,1 $\pm$ 53,1            |

\*Reliability as compared to parameters of vivarium control rats.

\*\*Reliability as compared to parameters of animals in synchronous [ground-based] experiment.

On the 6th day after the experiment the low activity of this enzyme persisted in both experimental groups--flight and synchronous--differing reliably from the vivarium control (see Table). It should be noted that activity of this enzyme in flight animals did not differ from activity in rats of the synchronous experiment immediately after landing and on L+6 (see Table). Analogous data had been obtained in experiments aboard Cosmos-782 and Cosmos-936 [6, 7].

Repeated immobilization stress, to which the animals were exposed, did not lower enzyme activity in flight and synchronous groups of rats, as compared to the vivarium control; however, we did demonstrate a decline in malic enzyme activity in flight rats, as compared to those in the synchronous control experiment (see Table).

These studies indicate that the decline of malic enzyme activity in the rat liver persists for the first 6 days of the postflight period; the test with repeated immobilization stress made it possible to demonstrate for the first time (unlike the findings made in the experiments aboard Cosmos-782 [6] and Cosmos-936 [7]) the effect of weightlessness on activity of one of the key enzymes of lipogenesis, malic enzyme.

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## DISCUSSIONS

UDC: 612.821.1/.3-06:613.863]:613.693

### METHODS FOR PILOTS AND CADETS TO RESOLVE FRUSTRATING SITUATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (manuscript received 24 Dec 82) pp 86-87

[Article by V. I. Yevdokimov]

[Text] It is known that investigation of resolution of frustrations helps understand the origin of neuroses, predict behavior of an individual under stress and in difficult aviation situations [3-7].

Our objective was to test the influence of methods of reacting to frustrating situations used by cadets and flight personnel on their achievement in practical flight training and quality of flight work.

#### Methods

We used the Rosenzweig test pictures as models of frustrating situations. The test consists of 24 pictures. On each of them there is one person that makes a statement that describes the frustration, whereas over the other people there is a blank box for responses. Without going into the theoretical conceptions of the frustration problem existing abroad, we shall offer the most complete definition of this concept, which can be considered a sort of validation of this method. Frustration is construed as "a person's state manifested by typical and distinctive feelings and behavior, which is elicited by objectively unsurmountable (or so construed subjectively) difficulties on the way toward a goal or solving a problem" [4].

In addition to the original Rosenzweig test, we used a variant consisting only of responses by the characters.

Each response of a subject was evaluated from the standpoint of direction and type of reaction [1, 6]. The following reactions were distinguished according to direction: a) extrapunitive, directed toward the animate and inanimate surroundings; b) intrapunitive, directed on oneself; c) impunitive, which are considered of little significance and responsive to correction at the time they occur. Reactions can be divided into the following types: a) obstacle-dominance, with fixation on an obstacle; b) ego-defense, with fixation on self-defense; c) need persistence, with fixation on satisfaction of needs.

These six categories combined offer nine possible rating factors.

## Results and Discussion

In order to obtain psychodiagnostic information with the Rosenzweig test, we submitted to correlation and factor analysis test results obtained in the first and then, 3 years later, fourth year of flight school training, with evaluation of practical flight training, discipline, general health status, results of neurological examination during expert medical certification for flight work, occupational screening, achievement in theoretical studies and index of sociometric status.

We found that the characteristics of the Rosenzweig test were stable in the 1st and 4th years of training and had statistically reliable positive links. This is indicative of reliability of the test and its demonstration of psychological distinctions; it is also consistent with the data of other researchers [2, 6]. Thus, it is possible to use this test in extended expertise of flight personnel and cadets.

In interpreting the test results, it was established that pilots and cadets often react extrapunitive in resolving frustrating situations, along with the ego-defense type of resolution of reaction. This shows that pilots and cadets are under some stress and that they are very demanding of their social environment. Such reactions could be attributed to the specifics of their work.

We set as a goal the study of the influence of different means of resolving frustrating situations on the quality of flight training. Using correlation analysis, it was established that an intrapunitive direction ( $r = 0.36$ ,  $P < 0.01$ ) of obstacle type of reaction ( $r = 0.23$ ,  $P < 0.1$ ) among 4th year cadets is instrumental in good achievement. The other test parameters had low correlative links to flight training achievement.

Perhaps, with the intrapunitive type of response (low and moderate values) with fixation on the obstacle, the subjects perceive their situation, shortcomings and mistakes properly. They resolve frustrating situations on their own. The frustrating factor seems to fix their attention and becomes the source of feelings and actions. For this reason, such cadets train more thoroughly for flights and perform them well.

The characteristics of the Rosenzweig test in the 1st year group of cadets presented significant links with the data from vocational screening. Intrapunitive and impunitive reactions are indicative of an adequate level of development of psychological personality processes ( $r = 0.36$ ,  $P < 0.01$ ;  $r = 0.26$ ,  $P < 0.05$ , respectively), which must be taken into consideration when experts are making vocational screening decisions.

Correlation analysis of results of the Rosenzweig test with evaluation of general health status and findings of neurologist's examination revealed that the relationship was low for virtually all test characteristics. There were close to significant links between impunitive ( $r = 0.24$ ,  $P < 0.1$ ) and extrapunitive ( $r = -0.25$ ,  $P < 0.05$ ) directions of reactions, on the one hand, and general

health status, on the other, which correlated positively with practical flight training achievement ( $r = 0.31$ ,  $P < 0.05$ ).

Similar data were obtained when we compared the test characteristics to theoretical achievement and index of sociometric status, which had a high correlation with flight achievement ( $r = 0.60$ ,  $P < 0.05$ ).

Factor analysis involved four factors. The first, which was called factor of general development, included (with high weight) achievement in general theoretical subjects, physical training, evaluation of vocational screening and index of sociometric status. This factor was represented with significant weight by practical flight achievement and intrapunitive direction of Rosenzweig test reaction.

The second factor consisted of statistically significant examination data from the Rosenzweig test for first year cadets. In addition, it included evaluation of vocational screening that was close to being statistically reliable and some screening tests. This confirms the results of correlation analysis, characterizing the negative influence of extrapunitive direction on mental processes relevant to flying.

The third factor showed the correlation between test characteristics of cadets examined in the 1st and 4th years of study.

The fourth factor, called flight achievement factor, contained statistically reliable weights of ratings of practical flight achievement, discipline and theoretical training in special navigation subjects. Weights of the index of sociometric status and evaluation of general health status were close to significant in this factor.

In order to determine whether it is possible to use a variant of the test consisting only of responses of persons in the pictures, we tested 78 senior cadets with this variant. Six months later, we showed them the pictures of the original test. The results were submitted to correlation analysis. We found that there were statistically significant positive intercorrelations for all characteristics of the original test and its textual variant. This means that, in the absence of Rosenzweig test pictures, it is possible to use its textual variant and the possibility of further modification is not ruled out.

In order to find the key of the coefficient of group conformity, we calculated the frequency of responses to test situations of 148 cadets and 67 pilots. An answer in which identical responses to situations were present in at least 40% of the cases was considered standard. As a rule, the responses coincided for pilots and cadets. The key for pilots differed from the group conformity of other groups [1, 5, 6], which could be attributed to the presence of specific, so-called, flight traits in flight personnel.

There was insignificant correlation between the coefficient of group conformity and index of sociometric status, and it was negative with flight achievement ( $r = -0.27$ ,  $P < 0.05$ ). This suggests, in the first place, that the test situations cannot fully reflect the specifics of relations in a group of pilots. In

the second place, it stresses the need to modify the test for flight personnel, which could be the subject of our future studies.

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## BOOK REVIEWS

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### NEW BOOK ON DIAGNOSTIC NYSTAGMOMETRY BY M. M. LEVASHOV

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 3, May-Jun 85 (signed to press 15 Apr 85) pp 87-89

[Review by A. A. Shipov of book "Nistagometriya v otsenke sostoyaniya vestibulyarnoy funktsii. Seriya 'Problemy kosmicheskoy biologii'" (Nystagmometry in Evaluation of Vestibular Function. "Problems of Space Biology" Series), Vol 50, by M. M. Levashov, edited by A. M. Ugolev, corresponding member of the USSR Academy of Sciences, chief editor of volume--V. A. Kislyakov, doctor of biological sciences, Leningrad, Nauka, 1984, 221 pages]

[Text] As we know, nystagmus is an important vestibulomotor reaction in otorhinolaryngological and neurological practice. The value of this reaction in diagnosing a number of diseases, as well as vocational screening, becomes particularly evident when it is recorded graphically and given a proper quantitative evaluation. However, the diversity of methodological approaches to such evaluation and sometimes their insufficient theoretical validation render the results of most tests performed to date virtually incomparable. It was high time for a classification of the characteristics of the nystagmic reactions used, optimization of existing tests of vestibular function, theoretical validation of empirically found procedures for studying nystagmus, determination of informativeness of different characteristics for diagnosis of diverse diseases.

The monograph by M. M. Levashov, who devoted many years to comprehensive and thorough investigation of nystagmus in order to make effective use of it in clinical practice, has solved the above problems to a significant degree. The book sums up not only the results of the author's studies, but the findings of many Soviet and foreign researchers.

The monograph follows a well conceived plan and consists of an introduction, four independent chapters and conclusion.

In the Introduction, the author offers a general definition of his chosen area of research--nystagmometry as an aggregate of theoretical and applied studies (physiological, clinical diagnostic, aerospace, cybernetic) combined by a common object of investigation, nystagmus, as well as a quantitative approach to its study. Nystagmometry in vestibulology is merely one of the areas of its application, and it is characterized by the fact that the study of nystagmus emerges as a means of examining the vestibular system. The author dwells

on the basic distinctions and properties of vestibular nystagmus, questions of suitability of nystagmus for analysis of spatial orientation and statokinetic stability of man, interaction of optic and vestibular systems, as well as different parts of the labyrinth, analysis of effect of extralabyrinthine factors on vestibular reactions, i.e., questions that are the subject of theoretical and experimental nystagmometry. But, nystagmometry can also be well-used to solve applied problems, such as development of quantitative methods for differential diagnostics, professional screening and evaluation of efficacy of therapeutic measures. The ultimate purpose of such tests is to make the diagnosis of normal and pathological vestibular system and, in the case of pathology, to further pinpoint and define the diagnosis (local or extensive pathological process, extent of vestibular dysfunction, etc.). As validly noted by the author, in order to solve applied problems of nystagmometry it is necessary not only to validate theoretically some of the empirically found procedures, optimization of vestibulometric tests, but to solve a number of technical problems--measured vestibular stimulation, reliable recording of nystagmus, automatic quantitative processing, etc.

From the Introduction, the reader can clearly see that, of the large range of problems referable to nystagmometry, the monograph includes only those that can serve as a source of new information about the function of the vestibular system as such, correlations between the vestibular system and other sensory systems. In addition, there is discussion of problems of enhancing the effectiveness of vestibular diagnostics, and special attention is given to tests for the detection of latent dysfunctions. An effort was made to define the directions of future nystagmometric studies that appear promising.

In Chapter 1, the author acquaints the reader with tonic and rhythmic vestibulo-oculomotor reactions. Most of it deals with rhythmic nystagmus, as a reaction that reflects interaction between the semicircular canals of the labyrinth. Information is furnished about the pathways and centers of nystagmus, systems of slow and rapid components, extinction phenomenon, as well as influence of different parts of the central nervous system on vestibulooculomotor reflexes. The author convincingly illustrates how nystagmometric characteristics can be used for differential diagnosis of level of central nervous system lesion, on the example of interaction between vestibular and auditory functions. In the same chapter, there is also discussion of the main problems that arise when using nystagmography: calibration, recording rotatory nystagmus, development of vestibulometric tests for quantitative evaluation of function of the vertical canals, otolith system, etc.

The chapter concludes with discussion of the significance of quantitative studies of nystagmic reactions to both investigation of mechanisms of nystagmus and development of new vestibulometric tests and diagnostic procedures.

Chapter 2 deals with optic-vestibular integration studied by means of nystagmometry. On the example of physiological experiments on animals, the author demonstrates the close functional link between vestibular and optokinetic nystagmus. He shows quite convincingly that oculomotor reactions to combined stimulation (vestibular and optokinetic) could be the basis for developing utterly new vestibular tests. In such tests, the subject of investigation would be mechanisms of interaction between the vestibular and optokinetic systems involved in forming a biologically purposeful reaction--vestibulo-optokinetic nystagmus.

Chapter 3, which is the central and most important one for applied research, deals with systematization of nystagmometric characteristics. It is shown that, when using the characteristics of nystagmus, it is necessary to make a clear statistical description of the norm and define the type of distribution of parameters of nystagmus.

Untraditional nystagmometric and multidimensional characteristics proposed by the author are of special interest to applied nystagmometry. Here too, he formulates some extremely important diagnostic rules.

Chapter 4 describes in detail a mathematical-logic model of a bithermal test. It is deemed promising to use the proposed model for the study of mechanisms of the phenomenon of directional dominance in its different manifestations, in particular, upon extinction of nystagmus. In addition, use of this model improves appreciably the informative value of the bithermal test, it provides answers to questions that traditional test interpretation cannot answer (demonstration of compensation, ruling out pathology, etc.).

In conclusion, the author discusses the prospects of using automated systems to record, process nystagmograms and make diagnoses. He lists the necessary conditions for this and the problems encountered on this route, which can be considered a new stage in development of nystagmometric studies.

The monograph is well-illustrated; there is a rather complete bibliography listing more than 500 references by Soviet and foreign authors.

The book by M. M. Levashov will be appreciated by a wide range of readers: clinical otoneurologists, physiologists, engineers concerned with problems of mathematical description and modeling of biological processes, specialists in aerospace medicine.

#### CURRENT EVENTS AND INFORMATION

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#### PROBLEMS OF AVIATION AND SPACE MEDICINE AND PSYCHOLOGY DISCUSSED AT FOURTEENTH GAGARIN LECTURES

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[Article by editorial board]

[Text] The 14th Gagarin Scientific Lectures were held in early April 1984 and dedicated to the 50th anniversary of the birth of Yu. A. Gagarin and to International Aviation and Cosmonautics Day. Plenary meetings were held in Zvezdnyy and at the Institute of Problems of Mechanics, USSR Academy of Sciences. There were more than 10 scientific sections within the framework of the lectures. In addition, there were concurrent student Gagarin lectures which drew a particularly large audience this year (more than 400 papers from 32 VUZ's).

The meetings of the section, "Problems of Aviation and Space Medicine and Psychology," convened on 5-9 April 1984 in the auditoriums of the Institute of Problems of Mechanics, USSR Academy of Sciences.

In the last 14 years, there has been much quantitative and qualitative development of the work of this section. While 10-20 papers were delivered at each of the first 5 lectures, at the 14th there were more than 100. The section made good use of a new form of work: more than half the papers were presented in the form of poster reports. The range of problems covered by the section has been expanding from year to year. The different meetings were devoted specifically to the problems that are the most pressing in different time frames: physiological effects of weightlessness, accelerations and altitude; space biology; clinical aerospace medicine; screening and training of flight personnel and other issues.

A. I. Burnazyan and Ye. I. Vorob'yev, deputy USSR ministers of health, Academician O. G. Gzenko and others spoke regularly on the results of biomedical and medical investigations at plenary meetings of the Gagarin lectures.

Since 1981, there have been meetings of two subsections, within the limits of this section: physiological and psychophysiological. In 1984, another subsection was added, aviation and space psychology.

In 1984, many scientists and specialists from institutions in Moscow, Moscow area, Leningrad, Kiev, Minsk, Chelyabinsk, Yerevan, Frunze, Krasnodar and other cities of the Soviet Union were active participants in the work of the section.

The general meeting of the section, which convened under the guidance of Academician O. G. Gazenko, chairman of the section office, was opened with a broadcast of the voice of Yuriy Alekseyevich Gagarin which had been taped during his speech before the launch of the Vostok-1 spacecraft on 12 April 1961.

Then the rather comprehensive papers of I. D. Pestov and A. M. Genin--"Bio-physical Validation of Methods of Simulating Weightlessness," G. N. Kryzhanovskiy--"Some Mechanisms of Formation of Physiological Reactions and Their Correction," Yu. G. Nefedov et al.--"Investigation of Ultrastructure of Bacteria and Their Sensitivity to Antibiotics, Conducted in the Soviet-French Cytos-2 Experiment," Yu. M. Zabrodin, N. V. Krylova and A. K. Bokovikov--"Methodological Problems of Assessing an Operator's Functional State During Training on Simulator," were delivered and discussed.

The section's work then continued at meetings of three subsections, the brief contents of which are described below.

Subsection 1: "Status and Prospects of Development of Methods Used in Aviation and Space Medicine" (headed by A. I. Grigor'yev, doctor of medical sciences, and I. D. Pestov, doctor of medical sciences; scientific secretary--G. S. Ratner, candidate of biological sciences).

A total of 39 papers and reports was delivered at the subsection meeting. A considerable part of the papers delivered at the subsection meeting dealt with the results of combined investigations and simulation (including mathematical modeling) of spaceflight factors, as well as development of methodological approaches that help detect latent forms of pathology in pilots and cosmonauts.

The paper of B. F. Asyamolov et al. submitted the results of combined physiological investigations with simulation of the acute period of man's adaptation to weightlessness. They traced the dynamics of parameters characterizing the functions of the cardiovascular system, autonomic vestibular stability, work on different psychophysiological levels, mental status, as well as physiological and hygienic evaluation of dynamics of nutritional status and two diets. The subjects spent 7 days under antiorthostatic ( $-10^\circ$  angle) hypodynamic conditions.

G. V. Myaginskiy et al. used water immersion (method of dry submersion) lasting 7 days as a model of weightlessness. The authors found that the acute period of adaptation to simulated weightlessness had an adverse effect on functional capacities of the oxygen transport system.

A comparative study of immunological reactivity of man during long-term antiorthostatic hypokinesia and the effect of weightlessness was made by a team of researchers under the guidance of I. V. Konstantinova. Analysis of the data obtained led to the assumption that there is less marked redistribution of T cells from the blood stream into bone marrow and tissue reservoirs with hypokinesia than in spaceflight.

L. G. Pozharskaya and B. V. Morukov used a set of methods to investigate hormonal regulation of calcium metabolism during long-term bedrest. The speakers believe that the observed increase in blood calcium concentration in the evening and at night, as well as the high blood levels of parathyroidin and calcitonin at this period, are related to change in motor activity and load on the skeletal-muscular system.

The report of V. B. Noskov and V. Yu. Semenov contained information on the results of studying fluid-electrolyte homeostasis and its hormonal regulation under antiorthostatic conditions with hypohydration of the body. Being in antiorthostatic position was associated with less marked changes in hypohydrated subjects.

Investigation of homeostasis of body fluids with simulation of fluid-salt loads, but only using a mathematical model, was the subject of V. V. Verigo and G. F. Ponomareva.

The next group of papers described methods that permit demonstration of resistance to different spaceflight factors and latent forms of pathology in flight personnel.

The paper of E. V. Lapayev et al. demonstrated the potential benefit of using a stand they developed for testing vestibular analyzer function when body fluids are redistributed in a cranial direction.

The possibility of detecting latent forms of vestibular dysfunction with rotatory and caloric tests was indicated in the paper of M. M. Levashov et al. Absolute values of parameters of the diagnostic model exceeding the range of the statistical norm and asymmetry of parameters were considered as signs of deviations.

Investigation of vestibular function using digital modeling on a computer was the topic of the paper of V. M. Gusev and V. A. Kislyakov. The "model" of vestibular disturbances consists of five module-units: semicircular canal system, otolith system, vestibular parts of the central nervous system and efferent motor pathways, dynamics of angular displacement of the body in space, transport object. According to the data these authors obtained, the grossest mistakes in the stabilization system occur under conditions of perturbances occurring in leaps with exclusion of the system of the semicircular canals, whereas in the mode of periodic properties this applies to exclusion of the otolith system.

V. B. Malkin et al. developed a combined functional test for detection of early forms of cardiovascular disease in essentially healthy people. Their paper provided physiological validation of the proposed method, in which subjects breathed with oxygen-deficient gas mixture (up to  $11.0 \pm 0.5\%$ ) and subsequently exercised on a bicycle ergometer. The clinical ergonomic approach to expert certification of flight personnel is being developed by B. I. Parmenov-Trifilov. He discussed in his paper methodological procedures for testing cardiovascular reactions of flight personnel on complex simulators and, in particular, approaches to evaluation of stability and instability of hemodynamic parameters as a manifestation of somatic and functional pathology.

V. P. Buzulina and V. S. Georgiyevskiy called attention in their paper to the need to make a more thorough analysis and calculations of the causes of deterioration of circulatory regulation, which has been found in postflight examinations of cosmonauts.

Mathematical modeling of hemodynamics in antiorthostatic position was the topic of the report of V. V. Rummyantsev and A. I. D'yachenko, and with exposure of man to accelerations, V. V. Mishenko et al. Interest was displayed in the papers and reports dealing with various metabolic distinctions during spaceflights (V. P. Bychkov, K. V. Smirnov, A. S. Ushakov and their coauthors), results of studying environments in pressurized areas and their effect on man (S. I. Zaloguyev, A. V. Sedov, Yu. P. Bizin, M. A. Vytchikova and their coauthors).

In his concluding remarks, A. I. Grigor'yev called the attention of the participants to the priority need to develop new methodological and methodical approaches to evaluation of the functional state of the body. The question of adequacy of physiological reactions to increase in load tests is important.

I. D. Pestov, in turn, stressed the fact that, at the present level of space medicine, more attention should be given to determination of general patterns of human body functions during spaceflights so that its reactions could be appropriately controlled, rather than to collection of factological material.

Subsection 2: "Mental and Physiological Factors in Flight Crew Performance" (headed by Prof G. M. Zarakovskiy and P. V. Simonov, corresponding member of the USSR Academy of Sciences; scientific secretary--V. A. Kurashvili, candidate of medical sciences).

A total of 24 papers (including poster reports) were delivered and discussed at meetings of this subsection, and they can be divided into 3 groups. The first group was concerned with problems of correlation between mental and physiological processes in the integral performance of a pilot, other crew members and mission control specialists. The second group consisted of methodological papers and the third, papers dealing with psychophysiology of the visual and other analyzers in man.

The typical element of papers in the first group was validation of two conceptions of self-regulation of the human psyche and body functions during flight work: one of them emphasizes dynamic regulation as related to modes and stages of flight and the other, adaptation to long-term living conditions. The paper of N. I. Frolov was the basis for the first group. Using extensive experimental material obtained during actual flights, the author validated the thesis concerning functional optimum of physiological reactions of the body as a manifestation of the function of the part of the integral physiological system of achieving the goal of activity that provides energy and plastic support of this process. He cited new data indicative of the extremely refined interaction of autonomic functions with man's intellectual activity. The experimental data submitted by B. I. Savchenko served as a distinctive supplement to this theoretically and practically important finding; he dealt with the influence of motives of achievement and avoidance on simulated pilot activities, as well as some concrete conditions that determine the professional work

capacity of pilots, when flying for crop-dusting purposes (Zh. I. Gritskovich, N. A. Razsolov), when exposed to strong photic stimuli (N. N. Zatsarnyy, A. I. Ivanov, L. N. Karelina) and others.

The second conception of self-regulation of mental and body functions in man was described in the paper of A. I. Koreshkin, "Basic Patterns of Physiological, Individually Acquired Adaptation--Deadaptation of Man to Environmental Changes." The author found several patterns and developed a mathematical model that ties adaptation parameters to new conditions (for example, during flights to contrasting climate and geographic zones) with different duration of exposure to base conditions.

Several of the papers in the first group were concerned with methods of regulating the functional state of pilots and cosmonauts: by autogenic stimulation (A. I. Skrypnikov), art (G. S. Pogosyan), special training in use of non-instrument cues (S. V. Aleshin, A. A. Vorona, M. G. Chernyakina). In this respect, the procedure of formation of rational algorithms of pilot work and corresponding mechanisms of supporting activity is of special interest; it was validated by V. I. Parmenov-Trifilov. Interestingly, an analogous method of improving the work of aviation physicians had been proposed by K. A. Pimenova and V. N. Razsudov.

With regard to papers in the second group, we should mention data on contact-free methods (speech and oculomotor reactions) of assessing human work capacity submitted by M. V. Frolov. A survey of equipment and diverse methods of studying tracking problems was provided by V. G. Volkov, N. N. Lebedeva and V. M. Mashkova. Generalizations were offered for a number of original procedures for testing visual perception under the specific conditions of flying work (V. V. Dement'yev, A. D. Dankov, V. N. Telezhnikov, A. A. Malofeyev and others).

The papers in the third group included one of the reports important to the design of flight vehicle controls about the manipulative capacities of the hand (M. I. Boyko, A. P. Sonin, N. S. Boyko). The main direction of papers in this group, however, was improvement of efficiency of visual work done by pilots (crew members). O. T. Batluyev expounded an interesting hypothesis on formation of graphic images and ensuing procedures for training pilots in visual observation. V. V. Chumakov demonstrated the distinctions of eye function when data are displayed on an electric panel. The patterns of changes in color perception with exposure to accelerations were shown by A. I. Buturlin, M. A. Tikhonov et al. The paper of I. A. Korsakov was of particular interest. In his exquisite experiments, he demonstrated the feasibility of external control (by cathodic or anodic polarization of the brain) of sensibility and discrimination criteria of the visual analyzer.

On the whole, the papers (both delivered orally and exhibited on posters) of both subsections were on a high scientific level. Inherently, there was validation of most of the advanced theses by solid experimental material. It must be stressed that the results of experimental research are finding wide application in aeronautical and astronautical practice.

Subsection 3: "Problems of Aviation and Space Psychology" (headed by G. T. Beregovoy, USSR pilot-cosmonaut, candidate of psychological sciences, and Prof V. A. Ponomarenko; scientific secretary--N. V. Krylova, candidate of biological sciences).

More than 150 people participated in the work of this subsection. A total of 16 papers was delivered and 17 poster reports were presented for discussion.

The main scientific directions of the papers were: questions of aviation psychology (first), concrete problems of space psychology (second), theoretical and experimental psychological studies conducted in the interests of aviation and space psychology (third).

The papers referable to the first direction dealt with problems of aviation psychology pertaining to screening and training of flying school cadets, methods of evaluating and preventing mental states in flight personnel.

Ye. D. Sokolova, A. Ch. Agayev and V. Yu. Selin conducted a dynamic study of cadets in civil aviation schools using psychodiagnostic methods in order to investigate psychological factors related to achievement of flying school students. A. G. Bystrova, I. V. Ryapolov and I. N. Satanovskaya submitted the results of a study of informativeness of methods used for professional screening of pilot engineers and pilot navigators in the civil aviation.

N. F. Luk'yanova and D. I. Shpachenko commented on a number of distinctions in personality questionnaires, which must be taken into consideration when drawing conclusions about examination results. Some parameters of their own studies were described, which make it possible to predict quality of sociopsychological adjustment during training in a flying school.

G. S. Mazanov, N. D. Suvorov, I. S. Budygin and N. I. Meshcheryakova developed methods of evaluating the functional state of test pilots and some means of extending professional work capacity of pilots. The investigation conducted by O. M. Zelenina revealed that there are five specific types of transport aviation flight personnel groups that differ in value orientations. The structure of value orientations of civil aviation pilots was identified.

S. G. Mel'nik and A. V. Shakula attempted to develop the ways and means of controlling the psychophysiological state of pilots at all stages of preparations for and performance of flights in order to prevent adverse mental states. V. M. Zvonnikov showed the means of mental self-regulation by pilots: use of autosuggestion formulas to affect the body, self-education, self-activation within the limits of modification of autogenic training; purposeful activation of conceptions of work by means of relaxideomotor training. It was found that pilots are able to use methods of mental self-regulation.

The results of testing spatial orientation and balance in space, and the correlation between these functions were submitted in the paper of T. P. Bodachenko, V. D. Yustova and O. P. Yakovlev. Development and use of some methodological procedures made it possible to gain information about the state of spatial orientation and balance function in flight personnel, and change in them during flight work.

The paper of A. S. Gozulov dealt with the effects of some characteristics of verbal communications on adequacy of operator's formation of image of air situation. Practical recommendations have been developed on standardizing forms of verbal communication in the air traffic control system.

The second direction is referable to the area of space psychology, psychological science, that is formed as a combined direction based on data obtained in general psychology (theoretical and experimental), aviation, engineering, social psychology and psychophysiology (B. F. Lomov). The papers referable to the second scientific direction confirm this thesis.

R. B. Bogdashevskiy made an attempt at disclosing the main guidelines, methods and means of psychological examination and development of the cosmonaut's personality.

V. A. Sutormin and M. L. Khachatur'yants described stress experiments, which simulated the work of cosmonauts in irregular, emergency situations, and their studies made it possible to demonstrate the distinctions of professional motivation.

K. K. Ioseliani, A. L. Narinskaya and Sh. R. Khisambeyev proposed a combined approach to evaluation of mental work capacity, which can be recommended for use in space psychophysiology at the cosmonaut screening and training stages. Use of psychophysiological characteristics of cosmonauts to predict their inflight work capacity was discussed by Ye. G. Singatulin and V. P. Zaval'nyuk.

K. K. Ioseliani and V. A. Shaposhnikov undertook development of a method of diagnosing mental work capacity of cosmonauts in flight, which is based on combined analysis of direct observation data and results of routine physicals.

Work, rest and sleep schedule during a spaceflight lasting 211 days was discussed by V. I. Myasnikov and V. I. Makarov.

The paper of O. P. Kozerenko et al. disclosed the role of socialization in optimizing cosmonauts' living conditions. There was discussion of optimization of cosmonauts' psychoemotional status using esthetic factors (O. P. Kozerenko, I. M. Raygorodskaya).

With reference to psychological aspects of cosmonaut performance on simulators, I. B. Solov'yeva devoted special attention to conformity of training and real conditions.

The results of theoretical and experimental psychological research were reflected in the materials of the third scientific direction.

The systems approach to operator achievement (F. B. Berezin) is based on combined investigation of the process of mental adjustment to conditions that impose greater demands on adaptation mechanisms. It includes the clinical method, psychodiagnostic testing methods, sociopsychological methods, electrophysiological methods, biochemical methods of studying humoral regulation and the traditional methods of engineering psychology.

Methodological aspects of evaluating the operator's state during training on a simulator were the topic of Yu. M. Zabrodin, N. V. Krylova and A. K. Bokovikov. They demonstrated the importance of the problem of achieving similarity of functional state in the training process and actual work.

V. I. Il'in reported on the results of a study of correlations between personality distinctions, behavioral sets and nature of hormonal regulation in the presence of some forms of endocrine pathology. This study made use of factors of subsequent cluster analysis on the basis of multifaceted examination of the personality.

The paper of L. D. Chaynova was concerned with functional comfort as the optimum state for an operator.

N. V. Krylova and A. K. Bokovikov submitted results of a study of operator performance in processing video information when time is short.

The studies of O. O. Ryumin dealt with the effect of shifts differing in duration for operators conducting visual and instrument observation on status of several physiological functions and work capacity of operators in work crews consisting of three people. Recommendations were offered for optimum organization of work and rest schedules for crews.

The paper of A. A. Bobrov and Ye. V. Migulina submitted results of experimental studies of the effect of central electroanalgesia on some psychophysiological parameters and performance of operators. Improvement of psychophysiological parameters was also associated with changes in electrophysiological parameters, which was indicative of elimination of mental tension. The purpose of the studies of T. B. Isayeva and A. A. Bezbogova was to demonstrate the possible relationship between quality of operator performance, working conditions and individual personality distinctions of operators.

The paper of D. A. Leont'yev was devoted to a description of two mechanisms of meaningful regulation of activity--personal meaning and meaning set. Questions of volitional regulation were discussed in the paper of V. A. Ivannikov. S. M. Morozov investigated the performance approach to the problem of mental regulation.

Guidelines for selecting small groups of specialists with consideration of their psychological compatibility were discussed by Yu. M. Bobrov.

I. V. Smirnov and N. V. Gavrilova submitted data on use of psychorelaxation techniques based on adapted methods of group transcendental meditation.

The paper of V. A. Zinochkin submitted the results of studies using the method of assessing balance function in parachutists. N. I. Moiseyeva et al. reported on studies of spatial and time orientation of delta glider pilots.

S. A. Varashkevich developed a universal unit of effector actions in a multiple testing procedure.

It is apparent from this brief survey of the work done by the subsection that the submitted materials reflected the main theoretical and practical developments in the field of space and aviation psychology.

The 15th Gagarin scientific lectures, scheduled for April 1985, will be dedicated to the 40th anniversary of the victory of the Soviet people in the Great Patriotic War, 25th anniversary of the cosmonaut training center and International Day of Aviation and Cosmonautics.

## OBITUARY

UDC: 613.693+629.78]:92 Isakov

PETR KUZ'MICH ISAKOV (1909-1984)

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[Article by editorial board]

[Text] Petr Kuz'mich Isakov passed away after a serious illness in his 76th year; he was a prominent specialist, scientist and pedagogue in the field of aviation and space medicine, doctor of medical sciences, professor, recipient of the USSR State Prize, chairman of the section of aviation and space medicine of the Moscow Physiological Society.

In his 45 years of service in aviation, P. K. Isakov made an inestimable contribution to the inception and development of Soviet aviation and space medicine.

P. K. Isakov was a scientific classicist and always strived for strictness and completion of his works, which were notable for clear and profound argumentation. His strong point as a scientist was concrete logical thinking, which was based on encyclopedic erudition and scientific facts.

The outstanding talent and industriousness of P. I. Isakov were manifested already at the very start of his life, when he successfully combined excellent studies at an institute, work as department assistant and fruitful scientific research.

P. K. Isakov was concerned with the most important problems of aerospace physiology, such as accelerations, G forces, hypoxia and psychophysiology of flight work.

Petr Kuz'mich was an excellent organizer of scientific research, remarkable administrator and educator of scientific personnel; he trained more than 20 candidates and doctors of medical sciences.

In the years of the Great Patriotic War, P. K. Isakov was directly involved in organizing medical support of combat operations of long-range aviation.

Many USSR orders and medals were bestowed upon P. K. Isakov for his services to the homeland.



Petr Kuz'mich devoted much attention to public service. He was repeatedly elected to the board of the Moscow Physiological Society, chairman of the section of aviation and space medicine of the Moscow Physiological Society, to the DOSAAF Committee; he was a member of the higher certification commission, chairman of the scientific council under the Committee for Physical Culture and Sports Affairs of the USSR Council of Ministers, etc.

P. K. Isakov was an ardent propagandist and popularizer of achievements of aerospace medicine; he regularly delivered lectures and papers at scientific conferences and congresses, within the framework of the All-Union Znaniye Society he spoke before scientific workers, pilots, commanders and aviation physicians. Petr Kuz'mich wrote the scripts for six popular science films, one of which was "Ivan Petrovich Pavlov."

Petr Kuz'mich was a witty conversationalist and always gave brief and pithy answers.

He was always true to his ideals, always had his own convictions and never turned from his chosen route.

Flying practice was the compass that Petr Kuz'mich always had in his field of vision.

He was sincere and spontaneous in his dealings with others. Petr Kuz'mich attracted both the old and the young. And for each he would find a special word, a special look, a special approach. He had the capacity to discover new people and find in them only what was inherent in them. He was exceptionally proper and decent, and he required this of others. Petr Kuz'mich accepted from his coworkers only true ideas and conceptions, and he firmly but politely rejected false ones. Self-seeking, compilation, subservience and lying were alien to him, he hated them and fought against them in others also without mercy.

Petr Kuz'mich could be angry, cheerful and sometimes bitter, but never insincere or dishonest. He was seldom harsh, but sometimes his silence was a considerably stricter criticism than public condemnation. His critical remarks were not discouraging; rather, they instilled hope since they were always constructive.

People not only listened closely to his words, but waited for them and sought them out. His very presence at a scientific meeting compelled speakers (regardless of their rank) to present their views with utmost responsibility.

P. K. Isakov was dedicated to science and equally dedicated to people. He knew all of his coworkers well, their strong and weak points, and knew much about each of them. Petr Kuz'mich was always himself, but he would become an organic part of the team of scientists, with whom he worked.

He was a universally gifted scholar, sensitive to everything new and progressive; he was made wise by the experience of a long life, in love with science, truth and people; he taught his coworkers to love and understand aviation medicine, delve into the deepest mysteries of human body functions during flights, to be just as truthful, honest and loyal to the homeland as he was.

To his last days, party-mindedness, purposefulness and an active vital position were inherent in him. The work of Petr Kuz'mich has left a deep mark on the work of many scientific groups and in aerospace medical science as a whole.

P. K. Isakov was a major scientific figure. The memory of Petr Kuz'mich--talented scholar, father of aerospace medicine, principled communist, sensitive and responsive friend--will remain forever in the hearts of those who knew him and worked with him.

SYNOPSIS OF ARTICLES FILED WITH THE ALL-UNION SCIENTIFIC RESEARCH INSTITUTE  
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RAT KIDNEY EXCRETORY FUNCTION UNDER ALTERED GAS CONDITIONS

[Synopsis of article by Z. B. Minina]

[Text] There are many works dealing with the effect of an altered gas atmosphere on renal excretory function; however, authors disagree as to the direction of changes in its parameters. It is known that the composition of excreted urine may be indicative of the nature of compensatory and adaptive reactions of the kidney. A study was made on 100 male albino rats of the levels of sodium and potassium in urine in order to assess tolerance to extreme hypoxia and hypercapnia. First all of the rats were divided into two groups (those sensitive to an audio signal and "inhibited" ones) on the basis of differences in force and degree of excitability of the central nervous system using the method of L. V. Krushinskiy. Four series of experiments were conducted. In the 1st (hypoxic) series, atmospheric rarefaction corresponding to an altitude of 9000 m was produced with daily increase by 3000 m for 3 days. In the 2d (hypercapnic) series, CO<sub>2</sub> concentration in the chamber was raised daily by 5% to an end value of 15%. In the 3d and 4th experimental series, stepped build-up of hypercapnia was combined with either build-up of hypoxia, analogously to the conditions in the 1st series, or stable 30% concentration of oxygen. There was a substantial decline in 24-h excretion of sodium and potassium in urine by the end of the exposure period in all series of experiments. At the end concentrations of CO<sub>2</sub> and O<sub>2</sub>, these parameters constituted 20-30 and 40-80%, respectively, of control values. There was more drastic decline of potassium concentration in urine with increase in hypoxia or hypercapnia, as compared to natriuresis. Urine Na/K coefficient was at a significantly lower level than in the control throughout the experiments. Fluid balance was low in the hypercapnia series of experiments with normal and low oxygen content in inhaled air, and somewhat increased as compared to normal gas conditions in the hypoxic series. Raising oxygen level to 30% in an atmosphere with high CO<sub>2</sub> content increased animal survival rate, normalized fluid-electrolyte balance and led to gradual rise of urine Na/K coefficient to the

control level. Weight loss of rats over the exposure period was minimal when there was a high O<sub>2</sub> content in the chamber atmosphere. Urine electrolyte levels in rats sensitive to audio signals were substantially lower on the 1st day of the test than in "inhibited" animals. These parameters leveled off under the extreme effect of hypoxia and hypercapnia. It is assumed that rats sensitive to audio stimuli are also less tolerant to extreme changes in the gas atmosphere. 1 table, 2 illustrations, 18 references.

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# EFFECT OF ACUTE HYPOXIA ON NATURE OF DEGRADATION OF MYOCARDIAL LIPIDS IN WHITE RATS DURING AUTOLYSIS

[Synopsis of article by G. A. Griбанov and S. A. Sergeyev]

[Text] Acute hypoxia (AH) and myocardial ischemia are associated with numerous disturbances in energetics of cells and significant functional disorders of various membrane structures (V. I. Shumakov et al., 1979; Opple, 1979). Most of these effects are mediated by the membrane lipid component. Changes in phospholipid metabolism are particularly significant (Vasdev et al., 1979; S. A. Sergeyev and G. A. Griбанov, 1981); they are related to activation of hydrolytic mechanisms and other reactions of lipid degradation and biotransformation. Intensification of catabolic reactions is observed with autolysis (both physiological and postmortem). There are extremely few concrete data about changes in lipid component of organs (in particular, the myocardium) during autolysis in the case of prior AH. Determination of the relevance of AH to lipid disturbances of the rat myocardium during autolysis was the purpose of this investigation.

We tested the effect of AH (1-h exposure in pressure chamber at P = 190 mm Hg) on the nature of autolytic changes in myocardial lipids (ventricular region) in albino rats. Autolysis was effected by a previously described method (G. A. Griбанov, 1977). Immediately after isolation and after 4, 10 and 24 h of incubation in a wet chamber under aseptic conditions at a temperature of 37°C, the tissue was homogenized in tris-saccharose buffer, pH 7.4, with 1 mM EDTA, and we determined the levels of total lipids, phospholipids, as well as qualitative composition and quantitative amounts of lipid fractions by the method of microfine-layer chromatography (G. A. Griбанov and S. A. Sergeyev, 1975; A. Griбанov et al., 1976).

The results of the investigation revealed that there was progressive increase, reaching 2.6-fold by the 24th h, in total lipids in the myocardium of "hypoxic" animals during autolysis, which is indicative of retention of synthetic potential of myocardial ultrastructures with regard to lipids. This was not associated with any change in qualitative composition of myocardial lipids. However, polyclycerophosphatides were not demonstrable among the phospholipids. Relative cholesterol content did not change appreciably in the course of autolysis in "hypoxic" rats, whereas the share of cholesterol esters increased already by the 10th h of autolysis, unlike control animals. Free fatty acid and triglyceride levels rose only by the 24th h of autolysis. Diglyceride

content during autolysis remained lower in "hypoxic" animals at all tested times (with the exception of baseline) than in control animals.

Among the myocardial phospholipid fractions, the greatest changes at the early stages (4 and 10 h) were referable to sphingomyelins, the levels of which dropped significantly, constituting 63.3 and 49.5% of base values, as well as phosphatidyl ethanolamines and phosphatidic acids, the amount of which progressively increased 1.9- and 3-fold, respectively. By the 10th h the concentrations of phosphatidyl cholines and lysophosphatides showed a tendency toward decline and constituted 76 and 43%, respectively.

At the late stages, the levels of most fractions returned to their base values, but there was considerable (3.9-fold) increase in share of glycerophosphate, with some decline in concentration of phosphatidic acids which, however, did not reach the base level. The fact that there was no increase in the important product of hydrolysis of phospholipids-lysophosphatides in the case of prior hypoxia is of some interest.

The obtained data indicate that AH preceding autolysis leads to changes in nature of catabolic degradation of endogenous lipids in the rat myocardium, delaying (inhibiting) at the early stage hydrolytic mechanisms of destruction of structural and metabolically active fractions. At the late stage, the usual hydrolytic pathways of degradation become involved (are activated), mainly of structural lipids-phospholipids, due to rapid dissociation of choline-containing fractions and lysophosphatides. 2 tables, 20 references.

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#### ARTERIAL PRESSURE AND ITS REACTION TO PHYSICAL LOADS AS RELATED TO DIFFERENT DEGREES OF DISTURBANCES OF GEOMAGNETIC FIELDS

[Synopsis of article by V. A. Kuz'menko]

[Text] It was previously shown that an increase in mean 24-h disturbance of the geomagnetic field (GMF) is associated with decreased excitability of hemodynamic regulatory mechanisms in healthy man in the absence of differences at rest. It was interesting to compare the state of the mechanisms of maintaining arterial pressure (BP) to disturbance of GMF during the actual hours of examination. For this purpose, we used data referable to 370 tests made 6 times a day on different days, on 20 essentially healthy men 18-30 years of age. BP was measured by the Korotkov method before and 40-60 s after compressing the bulb of a pneumatic dynamometer: 0.5 exertion in relation to maximum possible for a given subject lasting 1 min was monitored visually. During the measurements, the subjects were supine in a calm waking state. They were wakened for the night reading (at 4 am). The degree of GMF disturbance was characterized by 3-h K index from tables published several months later ("Kosmicheskiye dannyye" [Space Data], Izdatel'stvo "Nauka"). In our studies, GMF disturbance was unrelated to atmospheric pressure level or air temperature. The data were submitted to statistical processing.

According to individual data and averages for all subjects, we can distinguish 4 phases of changes in pressor reaction of BP to a test load in the range from minimal (K-1) to maximal (K-16) GMF disturbance: bimodal distribution. The reaction increased by 53% with change from K-3.5 to K-2 and by 55% with change from K-3.5 to K-5, according to mean data. The nature of GMF disturbance as a function of BP reaction was the same in the course of the day, although its mean level, intensity of different phases and position of extremes varied. Resting BP, which presented a marked circadian pattern, was unrelated to GMF disturbance. Thanks to baroreceptor control, variations of base BP level could affect excitability of central mechanisms and alter their dependence on GMF.

According to our data, base BP level in the range of its interindividual variations in healthy subjects is a nonlinear function of excitability of centers, which can be described by a curve with two maximums. With a BP fluctuating by  $\pm 1.4\%$  from the group mean, the reaction to the physical load was lowest according to mean value, and its phasic changes as a function of GMF were smooth: there was prevalence of attenuation of reaction as disturbance increased. With a base BP  $7 \pm 1.2\%$  below the group mean, the pressor reaction was higher by a mean of 74% and underwent the most changes as a function of GMF (100% range). With BP exceeding the group mean by  $6 \pm 1.3\%$ , the mean reaction was 55% higher, and the range of its phasic changes as a function of GMF constituted 90%. The curve describing these phasic changes was the same in shape as with low BP, but presented a shift in the direction of higher values for the K index.

It can be concluded that excitability of centers regulating BP, which was assessed by the reaction to a physical load, depends on base BP and GMF disturbance. Both functions were similar, with an M-shaped curve. Both moderate reduction and moderate increase in both factors, in relation to the mean level, were associated with heightened excitability of the centers. This similarity warrants the conclusion that the effects of GMF fluctuations on the tested parameters occur perhaps through change in afferent influx to the centers. We have yet to identify the mechanisms of this change and possible sources of signals. It must be borne in mind that the link between GMF disturbance and excitability of circulatory centers is dynamic, and it depends on the base state and time of day. 4 illustrations, 7 references.

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